QATAR UNIVERSITY

COLLEGE OF HEALTH SCIENCES

EFFECT MODIFICATION OF THE ASSOCIATION BETWEEN DIETARY PATTERNS AND DEPRESSION BY DIABETES AMONG ADULTS IN QATAR: A POPULATION-BASED STUDY

BY

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ABSTRACT

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Title: Effect Modification of the Association between Dietary Patterns and Depression by Diabetes among Adults in Qatar: a Population-Based Study

Supervisor of Thesis: Prof. Zumin, Shi.

Background: Diabetes is a major public health problem in Qatar and significantly increases the risk of depression. Dietary patterns are related to the incidence of depression among patients with diabetes. However, no study has been conducted in Qatar on the relationship between dietary patterns and depression symptoms in adults.

Aim: To assess the association between dietary patterns and depressive symptoms severity among adults with or without diabetes in Qatar.

Methods: 1000 adults were selected from the Qatar Biobank (QBB). Each person with diabetes was matched with one person without diabetes based on age and sex in this cross-sectional study. Food intake was assessed based on a computer-administered food frequency questionnaire (FFQ). Factor analysis was used to identify dietary patterns. Patient Health Questionnaire-9 (PHQ-9) was used to assess depression symptoms.

Results: Moderate to severe depression symptoms were present in 13.5% of the sample. Two dietary patterns were identified: “unhealthy” (high consumption of fast food, biryani, mixed dish (chicken/meat/fish), croissant) and “prudent” (high consumption of fresh fruit, salads/raw vegetables, canned/dried fruit, and dates). After adjusting for sociodemographic, lifestyle factors (smoking and physical activity), and chronic conditions, high intake of “unhealthy” pattern was associated with an increased prevalence of moderate to severe depression symptoms in individuals with diabetes (prevalence ratio, PR=1.41; 95% CI: 1.28, 1.56; p-value<0.001). While there was no statistically significant association between moderate to severe depression symptoms and the “prudent” dietary pattern among those with or without diabetes.

Conclusion: The “unhealthy” dietary pattern was positively associated with moderate to severe depression symptoms in those with diabetes. Promoting healthy eating habits should be considered in the prevention and management of depression.

Keywords Depression symptoms, Diabetes, Dietary pattern, Factor analysis.

DEDICATION

To my parents who have always encouraged me to work hard for the things that I aspire to achieve. To my loving brothers, my spiritual sister Fatima Al-Jassim and my classmate Nour Al-Hussaini for being there for me throughout the Master program.

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ABBREVIATIONS

IDF	International Diabetes Federation
MENA	Middle East and North Africa
SPMI	Serious and persistent mental illness
T2DM	Type 2 diabetes mellitus
IL- 6	Interleukin-6
CRP	C-reactive protein
HMW	High-molecular-weight
RR	Relative risk
HR	Hazard ratio
OR	Odds ratio
PR	Prevalence ratio
CI	Confidence interval
RCT	Randomized controlled trial
QBB	Qatar Biobank
PHQ-9	Patient Health Questionnaire-9
EPIC	European Prospective Investigation into Cancer and Nutrition
MET	Metabolic equivalent of task
PA	Physical activity
FFQ	Food frequency questionnaire
IRB	Institutional Review Board
HPA	Hypothalamic–pituitary–adrenal
BDNF	Brain-derived neurotrophic factor

Chapter 1: Introduction

Background

In this century, diabetes mellitus is one of the biggest problems and challenges in the healthcare system.[1] According to the "International Diabetes Federation" (IDF) estimation in 2019, globally 463 million adults between 20 and 79 years suffered from diabetes.[2] This represented 9.3% of adults in this age group. Moreover, in the same report by IDF, in 2019 the highest age-adjusted prevalence of diabetes in adults between 20 and 79 years was in the "Middle East and North Africa" (MENA) Region, which is 12.2%. Within the MENA region, Qatar had an even higher age-adjusted prevalence of diabetes (15.6%).[2] Diabetes is a set of metabolic illnesses characterized by hyperglycemia (high blood glucose) caused by abnormalities in insulin production, insulin action, or both. Most of individuals with diabetes are classified into one of two broad etiopathogenetic groups. In the first group, type 1 diabetes is caused by a total lack of insulin secretion. In the second group, type 2 diabetes, which is much more common, is caused by a combination of insulin resistance and an insufficient compensatory insulin secretory response.[3] As life expectancy increases, the prevalence of diabetes and its complications will increase. This will bring a new socio-economic challenge at different levels, including individual, societal, and governmental.[4]

Depression is defined as a continuous loss of interest or pleasure in activities that the individual ordinarily enjoys, sadness, and hopelessness followed by a failure to carry out daily activities for at least two weeks.[5] Depression is one of the most prevalent mental disorders worldwide, affecting 264 million people in all age groups.[6] Globally, depression is a major cause of disability. The life expectancy of those with "serious and persistent mental illness" (SPMI) drops by up to 20 years compared to people without SPMI, even after the risks of suicide and accidents are adjusted.[7-9]

The most common comorbidity among people with diabetes is depression. In the general population, it was estimated that the lifetime prevalence of major depression is

16.2%[10]. Based on a recent cross-sectional study, 15.4% of Qatari with diabetes had self-reported depressive symptoms.[11] However, among people with diabetes, the lifetime risk of depression is approximately doubled.[12, 13] On the other hand, studies have shown that depression could also lead to the development of T2DM. In a meta-analysis of 9 longitudinal studies, it was found that the relative risk of developing T2DM in people with depression is 37% higher than those without depression.[14] Thus, the relationship between diabetes and depression is likely to be bidirectional.[14] Co-existence of diabetes and depression is a major clinical challenge [15], which may lead to a deterioration of quality of life, poor self-management of diabetes, increased incidence of complications, and reduced life expectancy.[15]

Over the past decade, an increasing number of studies have been conducted to understand the association between dietary patterns and the risk of depression. Although the results of these studies were inconsistent, there seems to be a link between them. In a meta-analysis, it was found that a healthy dietary pattern (high consumption of fruits, vegetables, unrefined grains, olive oil, seafood, poultry, and low-fat dairy) was associated with a reduced risk of depression, but a Western pattern (high consumption of refined grains, red and/or processed meat, high-fat dairy products, sweets, and low consumption of vegetables and fruits) was associated with an increased risk of depression.[16]

Dietary patterns are related to the incidence of depression among patients with diabetes. In a multicenter randomized controlled trial in Europe, participants were randomly assigned to one of three dietary patterns ("Mediterranean" dietary pattern supplemented with mixed nuts, "Mediterranean" dietary pattern supplemented with olive oil, or low-fat dietary pattern (control group)).[17] Compared to the control group (low-fat dietary pattern), the “Mediterranean” diet with mixed nuts reduced the relative risk of depression in individuals with T2DM by 41%.[17]

Among Qatari adults who attended the Qatar Biobank Study, dietary patterns were associated with poor diabetes control among individuals with diabetes.[18] However, it is unknown whether dietary patterns are associated with depression in Qatar.

Rationale for this thesis

Diabetes is a significant health problem in Qatar and as 15.4% of Qatari diabetes patients had depressive symptoms.(11) Diabetes and depression commonly coexist, posing a significant clinical challenge and resulting in a worse health outcome.(19)

Rather than examining the effects of individual nutrients, this study examined the relationship between overall dietary patterns and depression in adults with and without diabetes. Existence shows that dietary patterns among diabetes patients are associated with an increased risk of developing depression.(17, 20) However, there has been no comparable study undertaken in Qatar. This will be the first study in Qatar to evaluate the relationship between dietary patterns and depression among individuals with and without diabetes.

Understanding the association between dietary patterns and depression symptoms among adults with and without diabetes would assist healthcare providers in gaining a better understanding of the function of nutrition in the prevention and treatment of depression. As a result, health issues associated with both conditions will be reduced, while the overall quality of life will be improved. Additionally, the findings will help design intervention programs which may alleviate the economic burden associated with these two conditions by reducing health service utilization.

Aim and objectives

The aim of this thesis is to assess the association between dietary patterns using factor analysis, and depressive symptoms severity among adults with or without diabetes in Qatar.

The objectives of this thesis:

- To quantify the prevalence of having moderate to severe depression symptoms among people with and without diabetes in Qatar.
- To evaluate the relationship between dietary patterns and moderate to severe depression symptoms among adults in Qatar.

- To assess the interaction between dietary patterns and diabetes in relation to moderate to severe depression symptoms.

Research Questions

- Is there any difference in the dietary patterns between adults with and without diabetes?
- What is the relationship between diabetes and depression symptoms among adults in Qatar?
- Is the association between dietary patterns and depression symptoms modified by diabetes status?

Hypothesis

We hypothesized that there is an association between unhealthy dietary pattern and depression symptoms severity, which is stronger among those with diabetes than those without diabetes.

Chapter 2: Literature Review

Bidirectional association between diabetes and depression

Diabetes is one of the world's major public health issues, and depression is a severe mental health problem that impairs quality of life and mental and physical functioning. A considerable number of studies were conducted and found a bidirectional relationship between depression and diabetes. In 2008, a meta-analysis of 20 prospective studies with 6916 incident cases of diabetes, depression is associated with a 60% (95% CI: 1.37–1.88) increase in relative risk of T2DM. (21) Meanwhile, in another meta-analysis of 20 studies with 6,414 incident cases of depression, T2DM is associated with a 15% (95% CI: 1.02-1.30) increase in relative risk of depression.(21) These findings were further confirmed by another meta-analysis in 2017.(22) The new study included 51studies. In 32 studies with diabetes as an outcome, patients suffering from depression were found to be at an increased risk of developing diabetes than those not suffering from depression (OR= 1.34; 95% CI: 1.23-1.46). In 24 studies with depression as an outcome, the meta-analysis suggested that individuals with diabetes had an increased risk of developing depression (OR= 1.28; 95% CI: 1.15–1.42) than those without diabetes.(22) Moreover, this bidirectional association could be due to common risk factors for the two conditions, including a high level of inflammatory biomarkers(23-26), physical inactivity, poor diet, and obesity. (27-31)

Consequences of depression on people with diabetes

Strong evidence indicates that depression could accelerate the incidence of diabetes complications. In 2019, in a systematic review and meta-analysis study of 22 longitudinal cohort studies, individuals with diabetes and depression had an increased risk of incident macrovascular diseases (for example, coronary artery disease, angina, and stroke) by 38% (95% CI:1.30, 1.47) and microvascular diseases (nephropathy, retinopathy, neuropathy, diabetic foot, and sexual dysfunction) by 33% (95% CI: 1.25, 1.41) as compared to those with diabetes and without depression.[32] Furthermore, the study found that complications of diabetes increased the risk of depression incidence by 14% (95% CI: 1.07, 1.21). Nevertheless, the risk of diabetes complications incidence in individuals with depression is greater than the risk of depression incidence in individuals with complications related to diabetes.[32]

In a longitudinal study of 11,525 veterans with T2DM, the mean hemoglobin A1c (HBA1c) was significantly higher in individuals with depression and diabetes as compared to individuals with diabetes but without depression (mean difference of 0.13; 95% CI [0.03; 0.22]; P=.008).[33] In addition, the role of depression in contributing to impaired glycemic control and raised complications of diabetes indicates mortality from diabetes could increase due to depression. A meta-analysis of 16 studies indicated a positive association between depression and mortality rates among people with diabetes.[34] When people with diabetes and depression were compared to those without depression, the risk of death from any cause rose by 46% (95% CI: 1.29, 1.66).[34] Furthermore, people with diabetes and depression had a 39% higher risk of cardiovascular mortality than those without depression, according to the same meta-analysis based on the outcomes of 5 studies.[34] Moreover, in a study that examined the associations between depression status in T2DM patients and mortality over 10 years, after adjusting for health habits, demographic, disease control measures, and clinical characteristics, depression was significantly associated with mortality that were unrelated to cardiovascular disease or cancer (HR=1.61; 95% CI: 1.17, 2.22) and all-cause mortality (HR=1.52; 95% CI: 1.25, 1.85). However, there was no significant association between major depression and cardiovascular disease (HR=1.27; 95% CI: 0.90, 1.78) or cancer (HR=1.0; 95% CI: 0.65, 1.53) deaths.[35]

The role of inflammation biomarkers

Inflammation is a factor that plays a role in the bidirectional relationship between depression and diabetes, based on the growing body of evidence. In 2015, a meta-analysis of 58 studies found that elevations in the levels of two inflammatory biomarkers, including interleukin (IL)-6 and the C-reactive protein (CRP), were associated with major depression.[23] In contrast, in a meta-analysis that observed the association between high levels of inflammatory biomarkers and the risk of T2DM.[24] Based on 10 prospective studies, it was found that elevated IL-6 levels were associated with T2DM risk (RR=1.31; 95% CI: 1.17–1.46). Furthermore, findings from 22 cohort studies suggested that elevated CRP levels were associated with an increased risk of T2DM (RR=1.26; 95% CI: 1.16–1.37).[24]

In 2014, a study was conducted in an ongoing national cohort of English adults with a sample of 4,955 adults ≥50 years.[25] During a 6-year follow-up, the hazard ratio (HR) for the incidence of T2DM in participants with high CRP levels and heightened symptoms of depression was significantly higher as compared to those with low CRP levels and low symptoms of depression (HR=2.03; 95% CI, 1.14–3.61) and the association was independent of comorbidities and body mass index (BMI).[25]

A cross-sectional study was conducted in Germany to determine the association between biomarkers of inflammation and symptoms of depression among patients with recently diagnosed diabetes (< 1 year).[26] It included 295 individuals with T2DM and 139 with type 1 diabetes. A positive association between two inflammatory biomarkers (CRP (coefficient=2.601; P-value= 0.008) and high-molecular-weight (HMW) /total adiponectin ratio (coefficient= 18.146; P-value= 0.001)) and depressive symptoms was found among T2DM participants. In comparison, among those with type 1 diabetes, they determined a positive association between blood levels of soluble intercellular adhesion molecule (sICAM)-1 and depressive symptoms (coefficient= 0.021; P-value= 0.035). However, after multiple adjustments, the relationship between HMW/total adiponectin and depressive symptoms persisted significantly only among T2DM participants.[26]

Factors that modify the association between diabetes and depression

Existing evidence suggests that many factors may play a role in the association between depression and diabetes. In a meta-analysis study that included 14 observational studies with 82,239,298 cases, it was confirmed that risk factors for comorbid depression in T2DM patients are insulin use (OR = 1.71; 95%CI, 1.18–2.48), complications related to diabetes (OR = 2.91; 95%CI, 1.76–4.82), and educational status (OR = 1.91; 95%CI, 1.30–2.81).(36) However, it was found that gender (OR = 0.56; 95%CI, 0.47–0.65), regular exercising (OR = 0.51; 95%CI, 0.27–0.96), current high social status (OR = 0.64; 95%CI, 0.47–0.88), and marital status (OR = 0.53; 95%CI, 0.34–0.83) are protective factors of comorbid depression in T2DM patients. In a subgroup analysis, it was found that age (≥60 years) is positively (OR = 1.63; 95%CI, 1.26–2.11) and smoking is inversely (OR = 0.72; 95%CI, 0.56–0.92) associated with comorbid depression in people with T2DM. Based on the findings, using insulin, having diabetic complications, a low educational level, and being female are risk factors for depression among those with diabetes; however, being married, having a job, and doing regular exercise are protective factors.(36)

There is an essential role for lifestyle factors in the etiology of T2DM and depression. It was found that people with depression are less likely to comply with the dietary recommendation and they are more likely to be physically inactive, which contributes to obesity. (27-31) Obesity is a known risk factor for the incidence of diabetes.(27-31) In a longitudinal study, it was found that individuals with diabetes and having depressive symptoms were less likely to follow the exercise and dietary recommendations as compared to individuals without diabetes and depressive symptoms.(37)

Antidepressant use and its association with glycemic control were examined in adults with diabetes in several studies. Levels of HbA1C were significantly increased with the usage of multiple antidepressant subclasses, suggesting that depression medications may be a risk factor for suboptimal glycemic control.(38)Moreover, long-term use of antidepressants was significantly associated with the risk of diabetes.[39]

The effect of nutrients on diabetes and depression

Diet is one of the lifestyles that could play a role in modulating gut microbiota, inflammation, and body composition. These are known factors related to depression, metabolic syndrome, and diabetes.[40-42]

It was found in some studies that depression was positively associated with carbohydrate consumption in both people with and without diabetes.[43, 44] In a cross-sectional study, patients with type 1 diabetes who favored carbohydrates over proteins had higher depression scores.[20] However, in one cross-sectional study, there was no relation between carbohydrate intake and depressive symptoms.[45] The connection between carbohydrates and depression was explained by the metabolism related to insulin.[46] Insulin is essential not only in regulating carbohydrate metabolism but also assists in the transportation of tryptophan in the brain. The presence of tryptophan is needed in the synthesis of serotonin, which is a neurotransmitter that has a potential role in mood modulation.[46] Based on that, carbohydrate consumption could be an attempt to self-medicate depression.

The association between fat consumption and depression has been examined by a few studies. Increased levels of depressive symptoms among type 1 diabetes patients were associated with substituting fats for proteins.[20]In a cross-sectional study that included 1794 Japanese male workers aged between 18 and 69 years, Nanri et al. found that fats intake was not associated with elevated depressive symptoms.[45] However, the types of fat rather than the total amount of fat intake are important determinants of health effects. For instance, high consumption of omega-3 fatty acids that are found in fatty fish was associated with a low risk of elevated symptoms of depression (OR: 0.47; 95% CI: 0.27, 0.83).[47] On the other hand, high intake of trans-fatty acids were associated with increasing incidence of depression (HR=1.42;

95% CI: 1.09, 1.84).[48, 49]

Protein is one of the macronutrients that has shown its effect on both depression and diabetes. Among type 1 diabetes patients in Finland, favoring protein over fats or carbohydrates was inversely associated with depressive symptoms.[20] Many RCTs investigated the effect of high protein intake (28% to 40% of total energy) and normal protein intake (15% to 19% of total energy) on diabetes outcomes.[50-53]The findings are inconsistent. Some suggested that a high protein diet was associated with decreasing HbA1C,[50] but other studies showed that high protein intake did not affect glycemic control.[51-53]

Micronutrient deficiencies, such as vitamins and minerals, have been linked to depression. In a review paper, Wang et al. found a positive association between being deficient in zinc and the risk of depression. Furthermore, use of zinc supplements is beneficial for depressive symptoms.[54] However, the association between magnesium and selenium deficiency and depression is not well understood due to a lack of high-quality studies, and existing studies are inconclusive.[54]In addition, vitamin B12 and folate deficiency were associated with depression in several studies.[55-57] In a meta-analysis, vitamin D deficiency has been shown to be positively associated with the risk of depression (HR = 2.21; 95%CI: 1.40, 3.49).[58]

The effect of food on diabetes and depression

The association between individual foods and depression/diabetes has been examined extensively. In a meta-analysis that included 22 studies and 9 of them covered depression, Psaltopoulou et al. found that high intakes of vegetables, fruits, wholegrain cereals, nuts, seeds, and pulses are associated with a lower risk of depression (RR= 0.68; 95% CI: 0.54, 0.86).[59] Fruits and vegetables contain high levels of antioxidants which are beneficial in preventing depression.[60, 61] It is known that oxidative stress can cause neuronal damage that leads to depression.[62] Fruits and vegetables are also rich in polyphenols, which may reduce the levels of inflammation and prevent depression.[63]Moreover, folate is found in large amounts in leafy vegetables, green vegetables, and citrus fruits as well as in dried legumes.[61]As mentioned above, folate is inversely associated with depression.[55-57]

Nuts contain omega-3 fatty acids, B vitamins such as B1, B2, B6, B12, and magnesium, which may have an effect on mental health.[64-66] B vitamins are essential for neurological function, and increasing the consumption of these vitamins may help alleviate depression symptoms.[65] Magnesium also plays a critical function in the nervous system through its effects on neurotransmitter release and metabolism.[65] A cross-sectional study in the Chinese population found an inverse relationship between increasing frequency of nuts intake and depression scores (OR for ≥4 times per week= 0.82; 95 percent CI: 0.73, 0.92, compared to < once per week).[67]

Whole grains are a rich source of fiber, and specifically, cereal fiber that improves insulin sensitivity and lipid profile, and reduction in inflammation markers.[68] A high intake of whole grains and cereal fiber had a significant protective effect on T2DM; they were associated with a 21% (95% CI: 13% to 28%) reduction in the relative risk of T2DM.[69] This is consistent with the relationship between inflammation markers and depression and diabetes.[23-26]In addition, high consumption of fish is associated with a lower risk of depression, which may be due to the high consumption of omega-3.[60, 70, 71]Olive oil or oleic acid intake was inversely associated with the risk of depression.[48, 72, 73]Furthermore, limited or no meat consumption was determined to be possibly associated with poor mental health.[74, 75] The benefit that could be possibly associated with moderate consumption of lean red meat is that it is a source of zinc that is inversely associated with depression,[76, 77]as well as its vitamin B12 content that is inversely associated with depression.[78]

On the other hand, high consumption of sweets, commercial baked goods, and fast food was found to be associated with a higher possibility of depression.(48, 61, 79, 80) The association between these foods and the risk of depression is likely due to a high content of trans-fatty acids, and their effects on gut microbiota. Trans-fatty acids are associated with pro-inflammatory changes, a reduction in HDL-cholesterol, and an increase in LDL-cholesterol. These harmful biological alterations caused by trans-fatty acids may contribute to potentially harmful effects on depression.(48) Furthermore, these types of foods are typically high in saturated fats, which may increase the production of free radicals and boost pro-inflammatory states.(81)

The effect of dietary patterns on diabetes and depression

People do not consume isolated nutrients; rather, they eat diets that consist of numerous foods with complex combinations of nutrients that are potentially highly interdependent and synergistic, making their separate effects difficult to study.(82)

There are two major approaches to classifying dietary patterns, which include posteriori and priori approaches. The posteriori approach determines dietary patterns using a data-driven approach(83). Factor analysis is one of the statistical methods that is used to derive dietary patterns based on the underlying interrelationships between the dietary components.(84)Other widely used statistical methods include cluster analysis and reduced rank regression. A priori approach determines dietary patterns based on current knowledge and pre-defined diet quality scores. (83) Examples of priori based dietary patterns include the “healthy eating index” and the “Mediterranean Diet score.”(83)

Dietary patterns are related to the incidence of depression among patients with diabetes. Evidence from a systematic review that included 24 independent cohorts suggests that healthy dietary patterns (high in whole grains, fruits, vegetables, legumes, olive oil, and fish) are associated with a lower risk of depression (OR ranged from 0.64 to 0.78 in a linear dose response fashion with P-value < 0.01).[85] In contrast, highest intake of unhealthy dietary pattern (high fatty foods and sugar) was associated with a higher risk of depression as compared to the lowest intake (OR = 1.58; 95% CI: 1.11, 2.23). [61]

A study was conducted to determine the effect of dietary patterns on depressive symptoms among type 1 diabetes patients. The authors found that the "fish and vegetables" pattern (high in fruits, vegetables, legumes, fish, and low in soft drinks) was associated with lower depression scores.[20] Likewise, the "Traditional" dietary pattern (high in potatoes, meat dishes, cold cuts, and sausages) was associated with lower depression scores. However, a "Sweet" dietary pattern, including ice cream, sweets, chocolate, and sweet pastry, was associated with higher levels of depressive symptoms.[20] In a multicenter randomized controlled trial in Europe, participants who were aged ≥ 55 years and at high risk of cardiovascular disease were randomized to one of three dietary patterns ("Mediterranean" dietary pattern supplemented with mixed nuts, "Mediterranean" dietary pattern supplemented with olive oil, and low-fat dietary pattern (control group)). The results suggested that a "Mediterranean" diet supplemented with mixed nuts was associated with reducing the relative risk of depression among patients with T2DM by 41% (95% CI: 0.36, 0.98) compared to the control group (low-fat dietary pattern).[17]

In 2014, a meta-analysis study of 13 observational studies found that healthy dietary patterns are associated with a reduced odds of depression (OR: 0.84; 95% CI: 0.76-0.92; p-value< 0.001). However, there was no statistically significant association between depression and the "Western" dietary pattern (OR: 1.17; 95% CI: 0.97-1.68; P-value= 0.094).[60] Moreover, in a meta-analysis that included 21 studies, it was found that highest intake of healthy dietary patterns (high consumption of vegetables, fruits, antioxidants, fish, whole grains, olive oil, low-fat dairy products, and reduced consumption of animal foods) was associated with reducing the incidence of depression as compared to the lowest intake (OR=

0.64; 95%CI: 0.57, 0.72).[16] On the other hand, highest intake of western/unhealthy dietary patterns (high intakes of processed meat, red meat, butter, high-fat dairy products, high-fat gravy, sweets, refined grains, and potatoes, and low consumption of vegetables and fruits) was associated with an increased risk of depression as compared to the lowest intake (OR= 1.18; 95%CI: 1.05, 1.34).[16]

The evidence regarding the association between "unhealthy" diets (rich in fatty foods and sugar) and increased symptoms of depression is less consistent.[85]In three prospective studies, it was found that long-term exposure to "unhealthy" diets predisposes people to depression,[61, 79, 86] whereas four prospective studies found no such association.[87-90]

Gaps in the literature

Overall, evidence for the association between depression and dietary patterns among people with diabetes is still scarce. Moreover, we found that there are contradictory results regarding the association between depression and nutrient intake and dietary patterns. This may be because chronic diseases like depression are multifactorial in nature and related to many nutrients and foods.[91]

No study has examined the association between dietary patterns and the risk of depression among people with diabetes in Arab countries, including Qatar. As dietary patterns are culturally specific, more studies are needed in diverse populations to examine the association between dietary patterns and the risk of depression among patients with diabetes.

Chapter 3: Methods

Design

This study was planned, performed, and reported in accordance with the "strengthening the reporting of observational studies in epidemiology–Nutritional Epidemiology" (STROBE-nut) guidelines.[92] It was a population-based cross-sectional study using data from the QBB study.

Study sample

Started in 2012, QBB study began as an ongoing population-based cohort study and recruits Qatari or non-Qatari adults aged ≥ 18 years and have resided in Qatar for ≥ 15 years. Participants were recruited through family and friends, social media, or via the internet.[93]

The analytical sample of the current study was selected from the Qatar Biobank database. Information on sociodemographic, lifestyle factors, food intake, chronic conditions including diabetes and depression was extracted.

The inclusion criteria for subjects were: adults between 18 to 75 years with and without diabetes attended QBB and had information on self-reported diabetes status. The exclusion criteria were pregnant/lactating women during the study period.

Sample size determination

The sample was randomly selected from the Qatar Biobank database and they were1000 participants. The study sample was divided into two groups, where the first group included 500 participants with self-reported diabetes and the second group included 500 participants without diabetes.

In this cross-sectional study, each participant with self-reported diabetes was matched with one participant without known diabetes based on age and sex. The use of the case-control approach is due to the following reasons: 1) We only have access to the data of 1000 participants for free. Selecting 500 participants will give us adequate sample power to assess the association between dietary patterns and depression among those with diabetes. 2) People with diabetes were older than those without diabetes. Without matching for age, this will result in a significantly lower mean age among those without diabetes than those with diabetes. Based on that, through matching, we had a comparable control group.

We have estimated the sample power based on the overall prevalence of depression in the study population (15.4%).[11] We hypothesized that the prevalence of depression is 10% and 20% in those with low and high intake of a certain dietary pattern. With the sample size of 500 in those with or without diabetes, the sample power is 88.2%.

Data and sources

Dietary patterns (exposure variable)

Qatar Biobank assesses the diet using a food frequency questionnaire that was developed based on consultation with local nutrition researchers, focus groups, and field assessment of the food environment locally.[94] A total of 102 food and beverage items were assessed based on a computer-administered FFQ. Depending on the nature of the food item, there are five or six frequency options. This diet questionnaire included a question about the frequency of eating from a common dish, reasons for modification in dietary habits recently (if applicable),and snacking between meals. Individual food intake one year prior to the survey was recoded into times per week .[94] The internal validity of the FFQ was evaluated before being used in the survey.[94] Using Spearman's rank correlation test, the internal validity of the FFQ was examined by comparing the frequency of consumption of broad categories of foods (fish, salads, snacks, chicken, fast/takeaway foods, meat) to the frequency of consumption of the total of the individual foods within the broad category. Correlations (rho) varied from 0.3 for snack consumption to 0.74 for fish consumption.[94] Dietary patterns were constructed using factor analysis. We chose this method because it is based on the correlations among foods.[95] This is a data driven method and may capture the cumulative effects of different dietary components in the overall diet.[96] For nutrition education and public health actions, this insight is vital.[96] On the other hand, there is another knowledge-based approach, known as the dietary quality score, which quantifies the diet's overall quality.[97, 98] They are typically established in accordance with a known healthy dietary pattern, or in accordance with pre-existing dietary guidelines for the general population or for the prevention of a particular dietary-related illness.[97, 98] The Healthy Eating Index is a well-known example of dietary quality scores.[99] One drawback of this strategy is that it does not capture the overall diet pattern.[98, 100] This is mainly because many dietary quality scores only consider a subset of the diet's components and do not take their associated structure into account. This knowledge-based index may not fit all the populations. For example, in the case of heavy metal food contamination, a high intake of vegetable and whole grain may not have the benefits expected.[101] In China, it has been shown that plant-based diet increases the risk of chronic kidney disease.[101] Based on this, we decided to use exploratory factor analysis.

Depression (outcome variable)

In QBB, the depression status of participants was assessed using the Patient Health Questionnaire (PHQ-9).[94] This self-reported questionnaire is designed to screen for depressive symptoms and is not intended to be diagnostic.[102] The PHQ-9 has nine statements regarding symptoms in the past 2 weeks, each with a four-choice response. The response ratings for each statement ranged from 0 (not at all) to 3 (nearly every day). A composite score was calculated based on the nine items. Following the recommendation, the score for depressive symptoms was classified as follows: no or minimum depression (0-4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), or severe (20-27).[102] We define participants as experiencing depression symptoms based on a widely used cut-off value of ≥10.[102] This specific cut-off point has been previously validated for defining clinically relevant depressive symptoms.[103-105] Based on that, we classified participants into two groups: those with PHQ-9 < 10 as having minimal depression symptoms and those with PHQ-9 ≥10 as having moderate to severe depression symptoms.

Diabetes status (effect modifier)

In the study, diabetes was defined as fasting glucose ≥ 7 mmol/dL, glycated hemoglobin (HbA1C) ≥ 6.5 %, or self-reported diabetes. The following questions were used to assess self-reported diabetes: "Has a doctor ever told you that you had or have diabetes?", "How old were you when your diabetes was first diagnosed?", and "Are you being treated for your diabetes? (1) No; (2) Don't know; (3) Prefer not to respond; (4) Diet; (5) Increased physical activity; (6) Tablets; (7) Insulin" and "Did you start taking insulin within a year after being diagnosed with diabetes?".

General information

In the Qatar Biobank study, participants completed a computer-administered health and lifestyle questionnaire that included questions about sociodemographic factors, current and past smoking habits, past and current health, occupational information, family history of health conditions, sleeping patterns, physical activity levels, mobile phone use, cognitive and psychological state, and reproductive health for women.[94] Most of the components of the questionnaire were from validated tools in other studies. For example, smoking history and family reproductive history were from the "European Prospective Investigation into Cancer and Nutrition" (EPIC) study, sleeping patterns questions from the UK Biobank study, mobile phone use from the "Cohort Study of Mobile Phone Use and Health" (COSMOS), and the level of physical activity was determined using the "International Physical Activity Questionnaire" (IPAQ).[94]

Anthropometric and biological measurements

Various anthropometric measurements were collected from each participant, including body weight, hip and waist circumferences, and height. In addition, blood samples were collected to measure 66 clinical biomarkers, including inflammation, vitamins, and minerals.[94]

Covariates

Based on the literature review[17, 20, 106] sociodemographic factors, lifestyle factors, and chronic conditions were treated as potential confounders. Education was categorized as low (<=secondary school), medium (professional or technical school), and high (university or above). Leisure-time physical activity was measured in metabolic equivalent (MET) hours per week to account for both the amount of time spent on activities and the intensity of them.[107] It was calculated by multiplying the amount of time spent in each activity by particular MET values derived from the "Compendium of Physical Activities."[108] Then we categorized Leisure-time physical activity as: sedentary/light activity (<10 MET-hours/week) and moderate/vigorous activity (≥10 MET hours/week).[109] On diet was categorized as yes or no. Smoking status was recoded as smokers, non-smokers, or ex-smokers. BMI was grouped as underweight (<18.5 kg/m^2), normal (18.5 to 24.9 kg/m^2), overweight (25.0 to 29.9 kg/m^2) or obesity (≥30 kg/m^2). Medication use for hypertension or diabetes was categorized as yes or no.

Statistical analysis

The demographic data and dietary patterns of the subjects were summarized using descriptive statistics. Continuous variables were reported as mean ± standard deviation (SD). Percentage values were used to represent categorical variables. The Chi-squared test was employed for categorical data, while ANOVA and unpaired t-test was utilized for continuous variables to make comparisons across groups.

Factor analysis was used to identify dietary constructs. Based on the previous studies using QBB data, food intake was collapsed into 38 groups before conducting factor analysis.[18] Sample adequacy was checked using the Kaiser–Meyer–Olkin (KMO) test. The results revealed a large KMO of 0.88, therefore factor analysis was considered appropriate. The number of dietary patterns was determined by 1) Eigenvalue >1, and items with factor loading |≥ 0.30|; 2) scree plot (Appendix A); and 3) interpretability based on Qatar food culture. Varimax rotation was used to help in interpretation by minimizing the correlation between factors. Each participant was assigned a dietary pattern score. The sum of the factor loading coefficients and standardized weekly frequency consumption of each food group linked with that pattern was used to determine the scores for each pattern. A higher factor score suggested that a person's diet was more similar to that dietary pattern. The factor scores were divided into tertiles (tertile 1 represented a low intake of the food pattern; tertile 3 represented a high intake of the food pattern).

As the prevalence of depression was above 10%, to determine the link between dietary patterns and depression, "Poisson regression" with robust variance was used to evaluate the association between dietary patterns and depression as prevalence ratios (PRs). In cross-sectional studies, PR is easier to interpret and communicate to non-epidemiologists than the OR.[(110)] Four models were used: "Model 1" was adjusted for age and gender; "Model 2" was adjusted for smoking, education, physical activity and on diet in addition to age and gender. "Model 3" was also adjusted for diabetes, while "Model 4" was additionally adjusted for BMI (continuous), and hypertension medication. Associations between intake of food groups and depression symptoms were assessed using a "Poisson regression" model, adjusting for all variables in Model 4. The fully adjusted model included 999 participants. It means that 99.9% of the participants had complete data. Thus, we did not conduct imputing of missing values. Moreover, a sensitivity analysis was carried out to check the association between dietary patterns and depression symptoms as a continuous variable.

We examined the multiplicative interaction between dietary patterns and diabetes by including a product term in the Poisson regression model. A p-value ≤ 0.05 was considered significant. Stata 17.0 software was used to conduct all statistical analyses.

Ethical approval

QBB gathered the data utilized in this study, and all participants gave their consent. Participation was entirely optional. Additionally, participants were given the entire freedom to leave the QBB project at any moment without facing any repercussions. QBB provides de-identified data in an anonymized electronic format for research purposes. To guarantee data security, the dataset was kept on a password-protected computer that only the lead investigator had access to. The data was treated confidentially in accordance with the terms of the agreement with the QBB, and its confidentiality was maintained throughout the study process and thereafter. The Qatar Biobank Ethics Committee's Institutional Review Board (IRB) permission was acquired (Appendix B). Additionally, Qatar University's IRB exemption was obtained.

Resources

This study was supported by the Qatar university’s student grant (QUST-2-CHS-2021-148).

Chapter 4: Results

Characteristics of the study participants

The mean age of the 1000 participants from QBB who were 18 years or older was 48.6 years (SD 10.5). In total, the prevalence of smoking was 15.2%. The sample population was well-educated, with around 75.7% holding postsecondary diplomas or university degrees. The majority of participants had a higher socioeconomic status, with 48.6% earning more than 20,000 QAR per month. Furthermore, 45.1% of participants reported that they were on a diet with no difference by diabetes status (Table 1).

Moderate to severe depression symptoms were higher among female and younger age (< 50 years) participants as compared to their counterparts. Moreover, moderate to severe depression symptoms were significantly higher among those with diabetes as compared to those without diabetes. (Table 1)

In comparison to those with minimal depression symptoms, individuals with moderate to severe depression symptoms had a higher level of supplement use and HbA1C% levels. The prevalence of obesity was very high in both those with moderate to severe depression symptoms (63.7%) and those with minimal depression symptoms (50.5%). Furthermore, the prevalence of using insulin was higher among those with moderate to severe depression symptoms (Table 1).

There was no difference in these sociodemographic, lifestyle variables, and chronic conditions among individuals with moderate to severe and minimal depression symptoms: nationality, smoking, education, income, physical activity level, using vitamin D, on diet, using diabetes medication other than insulin, and using hypertension medication. (Table 1).

Table 1. Characteristics of Participants According to Depression Symptoms (n=1000) [a]

Factor	Total	PHQ-9 < 10 (Minimal)	PHQ-9≥10 (Moderate to severe)	P-value [b]
N	1,000	865	135	
Age (years), mean (SD)	48.6 (10.5)	49.2 (10.5)	44.2 (9.6)	<0.001
Age group, n (%)				<0.001
< 50 years	501 (50.1)	410 (47.4)	91 (67.4)	
≥50 years	499 (49.9)	455 (52.6)	44 (32.6)	
Sex, n (%)				0.007
Female	500 (50.0)	418 (48.3)	82 (60.7)	
Male	500 (50.0)	447 (51.7)	53 (39.3)	
Nationality, n (%)				0.13
Non-Qatari	129 (12.9)	117 (13.5)	12 (8.9)	
Qatari	871 (87.1)	748 (86.5)	123 (91.1)	
Smoking, n (%)				0.30
Non	754 (75.4)	655 (75.7)	99 (73.3)	
Smoker	152 (15.2)	126 (14.6)	26 (19.3)	
Ex-smoker	94 (9.4)	84 (9.7)	10 (7.4)	
Education, n (%)				0.22
Low (<=secondary school)	242 (24.2)	217 (25.1)	25 (18.5)	
Medium (professional or technical school)	288 (28.8)	244 (28.2)	44 (32.6)	
High (university or above)	469 (46.9)	403 (46.6)	66 (48.9)	
Missing	1 (0.1)	1 (0.1)	0 (0.0)	
Total monthly income (QR), n (%)				0.12
Less than 10,000	172 (17.2)	152 (17.6)	20 (14.8)	
Between 10,000 and 20,000	207 (20.7)	170 (19.7)	37 (27.4)	
More than 20,000	486 (48.6)	425 (49.1)	61 (45.2)	

Factor	Total	PHQ-9 < 10 (Minimal)	PHQ-9≥10 (Moderate to severe)	P-value [b]
Missing	135 (13.5)	118 (13.6)	17 (12.6)	
BMI (kg/m2), mean (SD)	31.0 (6.1)	30.7 (5.9)	32.8 (7.0)	<0.001
BMI categories, n (%)				0.012
Underweight (<18.5 kg/m^2)	4 (0.4)	3 (0.3)	1 (0.7)	
Normal (18.5 to 24.9 kg/m^2)	136 (13.6)	127 (14.7)	9 (6.7)	
Overweight (25.0 to 29.9 kg/m^2)	337 (33.7)	298 (34.5)	39 (28.9)	
Obese (≥30 kg/m^2)	523 (52.3)	437 (50.5)	86 (63.7)	
PA (MET hours/week), mean (SD)	663.2 (1833.5)	663.3 (1840.4)	662.1 (1796.0)	0.99
PA (MET hours/week), n (%)				0.71
Sedentary/light (<10 MET-hours/week)	768 (76.8)	666 (77.0)	102 (75.6)	
Moderate/vigorous (≥10 MET hours/week)	232 (23.2)	199 (23.0)	33 (24.4)	
Fasting Glucose, mean (SD)	7.6 (3.9)	7.5 (3.7)	8.0 (4.5)	0.20
HbA1C%, mean (SD)	7.0 (1.9)	6.9 (1.9)	7.3 (2.1)	0.019
Diabetes, n (%)	512 (51.2)	429 (49.6)	83 (61.5)	0.010
Using Supplements, n (%)	290 (29.0)	236 (27.3)	54 (40.0)	0.002
Using Vitamin D, n (%)	398 (39.8)	339 (39.2)	59 (43.7)	0.32
On Diet, n (%)	451 (45.1)	389 (45.0)	62 (45.9)	0.84
Using diabetes medication other than insulin, n (%)	359 (35.9)	310 (35.8)	49 (36.3)	0.92
Using Insulin, n (%)	160 (16.0)	129 (14.9)	31 (23.0)	0.018
Using Hypertension medication, n (%)	216 (21.6)	185 (21.4)	31 (23.0)	0.68

Note. PA= Physical activity, MET=metabolic equivalent, QR= Qatari Riyal

[a] Data from Qatar Biobank. Values for continuous measures presented as mean ± standard deviation and for categorical measures as n (%).

[b] Significance between individuals with moderate to severe and minimal depression symptoms. Chi-squared test for categorical variables and Unpaired t-test for continuous variables.

Prevalence of depression symptoms

Moderate to severe depression symptoms was found to be prevalent in the sample with a proportion of 13.5% (16.2% and 10.7% in those with and without diabetes, respectively). Additionally, 12.1% of individuals with diabetes reported experiencing moderate depression symptoms, while 4.1% reported experiencing moderately severe to severe depression symptoms. However, 7.8% of individuals without diabetes reported having moderate symptoms of depression, while 2.9% reported having moderately severe to severe depression symptoms (Figure1).

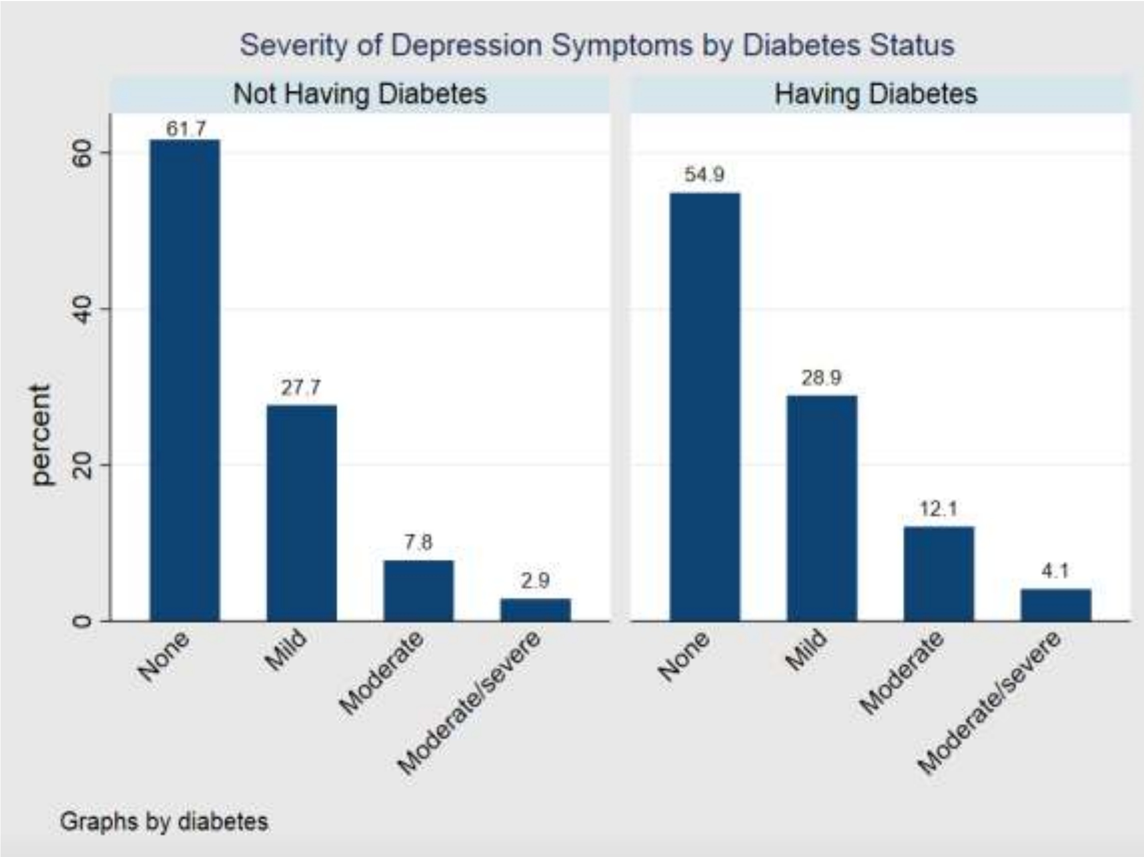


Figure 1. Severity of depression symptoms by diabetes status

Note. Moderate/ severe= Moderately severe to severe, (0-4= None) (5-9= Mild) (10-14= Moderate) (15-27= Moderately severe to severe)

Dietary patterns

We identified two dietary patterns. These patterns explained a total of 26.2% variance in the total food intake (15.3% in the first and 10.9% in the second patterns). The factor loadings for each pattern are shown in Table 2. Pattern 1 (“Unhealthy” pattern) was characterized by a high intake of fast food, Biryani, mixed dish (chicken/meat/fish), croissant, soft drinks, Lasagna, Zaatar fatayer, Arabic/Iranian bread, and white bread. On the other hand, pattern 2 (“prudent” pattern) was characterized by a high intake of fresh fruit, salads/raw vegetables, canned/dried fruit, and dates, fresh fruit juice, salads and cooked vegetables, brown bread, and soups/starters. Food groups and their constituents are listed in (Appendix C).

Table 2. Factor Loadings of Dietary Patterns

Variable	Unhealthy pattern	Prudent pattern
Fast food	0.70	
Biryani	0.66	
Chicken/meat fish mixed dish	0.61	
Croissant	0.58	
Soft drinks	0.56	
Lasagna	0.56	
Zaatar fatayer	0.55	
Arabic/Iranian bread	0.54	
White bread	0.52	
Ice-cream	0.49	
Red meat	0.48	
Desserts	0.48	
Asian noodle	0.47	
Potato	0.43	
Chicken	0.39	
Chocolate	0.38	
Butter	0.35	

Variable	Unhealthy pattern	Prudent pattern
White rice	0.34	
Cheese	0.33	
Other bread	0.33	
Eggs	0.32	
Tea	-	
Milk shakes	-	
Coffee	-	
Milk	-	
Salads and raw vegetables		0.71
Fresh fruit		0.70
Canned/dried fruit and dates		0.63
Fresh fruit juice		0.54
Salads and cooked vegetables		0.54
Brown bread		0.52
Soups/starters	0.44	0.51
Grilled/fried/baked Fish		0.49
Fish		0.47
Nuts		0.44
Yoghurt		0.37
Breakfast Cereal		0.33
Milk added to cereal	-	-
Variance explained (%)	15.3%	10.9%

Characteristics of the study participants according to dietary patterns

Sample characteristics according to the tertiles of dietary patterns are presented in Table 3. There were significant differences in age, education, depression, and vitamin D supplement use across the tertiles of the “prudent” and “unhealthy” patterns. Age and education were inversely associated with the “unhealthy” pattern, whereas they were found to be positively associated with the “prudent” pattern. Women were more likely to have a prudent pattern than men. The prevalence of smoking was higher in those with a high intake of “unhealthy” dietary pattern as compared with those with a low intake (20.7% vs 8.4%). The corresponding figures were 19.8% and 11.7% in those with low and high intakes of the “prudent” dietary pattern. The depression symptoms score was positively associated with the “unhealthy” pattern, but negatively associated with the “prudent” pattern. Across the tertiles of the “unhealthy” dietary pattern, the prevalence of moderate to severe depression symptoms was 7.8%, 12.3%, and 20.4%, respectively. The corresponding figures were 19.2%, 8.8%, and 12.6%, respectively, across the tertiles of the “prudent” dietary pattern. The prevalence of “on diet” increased with the increase of intake of the “prudent” dietary pattern. The prevalence of using diabetes medication other than insulin increased across the tertiles of the “prudent” dietary pattern. However, the prevalence of using insulin was increased across the tertiles of the “unhealthy” dietary pattern, while using hypertension medication decreased in the same pattern.

Table 3. Characteristics of Participants According to the Tertiles of Dietary Patterns (n=1000) [a]

Factor	Total	Unhealthy				Prudent			
		T1	T2	T3	P-value [b]	T1	T2	T3	P-value [b]
N	1,000	334	333	333		334	333	333	
Age (years), mean (SD)	48.6 (10.5)	52.6 (8.4)	48.9 (10.3)	44.1 (11.0)	<0.001	45.2 (10.6)	49.5 (10.3)	51.0 (9.8)	<0.001
Age group, n (%)					<0.001				<0.001
< 50 years	501 (50.1)	101 (30.2)	168 (50.5)	232 (69.7)		219 (65.6)	146 (43.8)	136 (40.8)	
≥50 years	499 (49.9)	233 (69.8)	165 (49.5)	101 (30.3)		115 (34.4)	187 (56.2)	197 (59.2)	
Sex, n (%)					0.072				<0.001
Female	500 (50.0)	181 (54.2)	168 (50.5)	151 (45.3)		138 (41.3)	182 (54.7)	180 (54.1)	
Male	500 (50.0)	153 (45.8)	165 (49.5)	182 (54.7)		196 (58.7)	151 (45.3)	153 (45.9)	
Nationality, n (%)					0.008				<0.001
Non-Qatari	129 (12.9)	56 (16.8)	44 (13.2)	29 (8.7)		67 (20.1)	37 (11.1)	25 (7.5)	
Qatari	871 (87.1)	278 (83.2)	289 (86.8)	304 (91.3)		267 (79.9)	296 (88.9)	308 (92.5)	

Factor	Total	Unhealthy				Prudent			
		T1	T2	T3	P-value [b]	T1	T2	T3	P-value [b]
Smoking, n (%)					<0.001				0.050
Non	754 (75.4)	270 (80.8)	245 (73.6)	239 (71.8)		235 (70.4)	257 (77.2)	262 (78.7)	
Smoker	152 (15.2)	28 (8.4)	55 (16.5)	69 (20.7)		66 (19.8)	47 (14.1)	39 (11.7)	
Ex-smoker	94 (9.4)	36 (10.8)	33 (9.9)	25 (7.5)		33 (9.9)	29 (8.7)	32 (9.6)	
Education, n (%)					<0.001				0.011
Low (<=secondary school)	242 (24.2)	98 (29.3)	83 (24.9)	61 (18.3)		70 (21.0)	90 (27.0)	82 (24.6)	
Medium (professional or technical school)	288 (28.8)	78 (23.4)	90 (27.0)	120 (36.0)		115 (34.4)	96 (28.8)	77 (23.1)	
High (university or above)	469 (46.9)	157 (47.0)	160 (48.0)	152 (45.6)		149 (44.6)	146 (43.8)	174 (52.3)	
Missing	1 (0.1)	1 (0.3)	0 (0.0)	0 (0.0)		0 (0.0)	1 (0.3)	0 (0.0)	
Total monthly income (QR), n (%)					0.67				0.79
Less than 10,000	172 (17.2)	56 (16.8)	64 (19.2)	52 (15.6)		63 (18.9)	57 (17.1)	52 (15.6)	
Between 10,000 and 20,000	207 (20.7)	70 (21.0)	65 (19.5)	72 (21.6)		66 (19.8)	68 (20.4)	73 (21.9)	

Factor	Total	Unhealthy				Prudent			
		T1	T2	T3	P-value [b]	T1	T2	T3	P-value [b]
More than 20,000	486 (48.6)	155 (46.4)	158 (47.4)	173 (52.0)		164 (49.1)	153 (45.9)	169 (50.8)	
Missing	135 (13.5)	53 (15.9)	46 (13.8)	36 (10.8)		41 (12.3)	55 (16.5)	39 (11.7)	
BMI (kg/m2), mean (SD)	31.0 (6.1)	30.7 (5.7)	31.5 (6.0)	30.9 (6.6)	0.23	30.9 (6.2)	31.7 (6.6)	30.5 (5.5)	0.024
BMI categories, n (%)					0.18				0.17
Underweight (<18.5 kg/m^2)	4 (0.4)	0 (0.0)	2 (0.6)	2 (0.6)		2 (0.6)	2 (0.6)	0 (0.0)	
Normal (18.5 to 24.9 kg/m^2)	136 (13.6)	45 (13.5)	37 (11.1)	54 (16.2)		52 (15.6)	36 (10.8)	48 (14.4)	
Overweight (25.0 to 29.9 kg/m^2)	337 (33.7)	125 (37.4)	111 (33.3)	101 (30.3)		115 (34.4)	103 (30.9)	119 (35.7)	
Obese (≥30 kg/m^2)	523 (52.3)	164 (49.1)	183 (55.0)	176 (52.9)		165 (49.4)	192 (57.7)	166 (49.8)	
PA (MET hours/week), mean (SD)	11.1 (30.6)	10.0 (26.4)	10.6 (31.2)	12.6 (33.7)	0.53	10.1 (31.5)	12.8 (35.2)	10.3 (24.0)	0.46
PA (MET hours/week), n (%)					0.43				0.64
Sedentary/light (<10 MET-hours/week)	768 (76.8)	258 (77.2)	262 (78.7)	248 (74.5)		262 (78.4)	251 (75.4)	255 (76.6)	

Factor	Total	Unhealthy				Prudent			
		T1	T2	T3	P-value [b]	T1	T2	T3	P-value [b]
Moderate/vigorous (≥10 MET hours/week)	232 (23.2)	76 (22.8)	71 (21.3)	85 (25.5)		72 (21.6)	82 (24.6)	78 (23.4)	
Fasting Glucose, mean (SD)	7.6 (3.9)	7.4 (3.5)	7.6 (3.8)	7.8 (4.2)	0.56	7.5 (3.8)	7.7 (4.1)	7.6 (3.6)	0.77
HbA1C%, mean (SD)	7.0 (1.9)	6.9 (1.8)	7.0 (1.9)	7.0 (2.0)	0.48	6.9 (2.0)	7.0 (1.9)	7.0 (1.8)	0.85
Depression score, mean (SD)	4.6 (4.5)	3.7 (3.9)	4.5 (3.9)	5.7 (5.3)	<0.001	5.4 (5.2)	4.0 (3.7)	4.4 (4.4)	<0.001
Depression symptoms severity, n (%)					<0.001				0.005
None (0-4 points)	582 (58.2)	224 (67.1)	189 (56.8)	169 (50.8)		178 (53.3)	203 (61.0)	201 (60.4)	
Mild (5–9 points)	283 (28.3)	84 (25.1)	103 (30.9)	96 (28.8)		92 (27.5)	101 (30.3)	90 (27.0)	
Moderate (10–14 points)	100 (10.0)	20 (6.0)	34 (10.2)	46 (13.8)		44 (13.2)	23 (6.9)	33 (9.9)	
Moderately severe to severe (15–27 points)	35 (3.5)	6 (1.8)	7 (2.1)	22 (6.6)		20 (6.0)	6 (1.8)	9 (2.7)	
Depression symptoms (PHQ-9≥10), n (%)	135 (13.5)	26 (7.8)	41 (12.3)	68 (20.4)	<0.001	64 (19.2)	29 (8.7)	42 (12.6)	<0.001
Diabetes, n (%)	512 (51.2)	169 (50.6)	176 (52.9)	167 (50.2)	0.76	163 (48.8)	178 (53.5)	171 (51.4)	0.48
Using Supplements, n (%)	290 (29.0)	86 (25.7)	101 (30.3)	103 (30.9)	0.27	88 (26.3)	101 (30.3)	101 (30.3)	0.42

Factor	Total	Unhealthy				Prudent			
		T1	T2	T3	P-value [b]	T1	T2	T3	P-value [b]
Using Vitamin D, n (%)	398 (39.8)	156 (46.7)	126 (37.8)	116 (34.8)	0.005	107 (32.0)	135 (40.5)	156 (46.8)	<0.001
On Diet, n (%)	451 (45.2)	174 (52.4)	142 (42.6)	135 (40.5)	0.006	125 (37.7)	152 (45.6)	174 (52.3)	<0.001
Using diabetes medication other than insulin, n (%)	359 (35.9)	128 (38.3)	128 (38.4)	103 (30.9)	0.069	102 (30.5)	127 (38.1)	130 (39.0)	0.042
Using Insulin, n (%)	160 (16.0)	41 (12.3)	54 (16.2)	65 (19.5)	0.038	55 (16.5)	53 (15.9)	52 (15.6)	0.95
Using Hypertension medication, n (%)	216 (21.6)	97 (29.0)	72 (21.6)	47 (14.1)	<0.001	63 (18.9)	76 (22.8)	77 (23.1)	0.33

Note. PA= Physical activity, MET=metabolic equivalent, QR=Qatari Riyal

[a] Data from Qatar Biobank. Values for continuous measures presented as mean ± standard deviation and for categorical measures as n (%).

[b] Significance between individuals with and without diabetes. Chi-squared test for categorical variables and ANOVA for continuous variables.

Univariate Analysis Results

Table 4 shows the results of the univariate analysis, which revealed a statistically significant association between the unhealthy eating pattern and moderate to severe depression symptoms (p-value <0.001). In comparison to the lowest tertile of the "unhealthy" pattern, the highest tertile was associated with a high prevalence of moderate to severe depression symptoms (PR=2.62, 95% CI 1.71-4.02). For the "prudent" dietary pattern, the highest tertile was associated with a 66% reduction in the prevalence of moderate to severe depression symptoms (95% CI 0.46, 0.94) when compared to the lowest tertile, but no significant trend was observed across tertiles (p for trend 0.348).

There was no statistically significant association between moderate to severe depression symptoms and race, education, income, smoking, leisure-time physical activity, non-insulin diabetes medication, and hypertension medication.

However, a clear association was observed between moderate to severe depression symptoms and age, gender, BMI, diabetes, and insulin use. The prevalence of depressive symptoms was lower among males and those aged >= 50 as compared to their counterparts. However, participants with diabetes, those on insulin, and those with an increasing BMI had an increased prevalence of moderate to severe depression symptoms.

Table 4. Univariate Analysis of the Main Outcome (Depression Symptoms) and Predictors

Moderate to severe depression symptoms	PR	95% CI	P-value [a]
Unhealthy pattern	1.35	1.23, 1.48	<0.001
Unhealthy pattern (tertiles)			
T2	1.58	0.99, 2.52	0.055
T3	2.62	1.71, 4.02	<0.001
Prudent pattern	0.91	0.74, 1.11	0.348
Prudent patten (tertiles)			

Moderate to severe depression symptoms	PR	95% CI	P-value [a]
T2	0.45	0.30, 0.69	<0.001
T3	0.66	0.46, 0.94	0.022
Race			
Qatari	1.52	0.86, 2.67	0.146
Age	0.96	0.95, 0.98	<0.001
Age group			
≥50 years	0.49	0.35, 0.68	<0.001
Sex			
Male	0.65	0.47, 0.89	0.008
Education			
Medium (professional or technical school)	1.48	0.93, 2.34	0.096
High (university or above)	1.36	0.88, 2.10	0.162
Total monthly income (QR)			
Between 10,000 and 20,000	1.54	0.93, 2.55	0.095
More than 20,000	1.08	0.67, 1.73	0.752
Smoking			
Smoker	1.30	0.88, 1.93	0.190
Ex-smoker	0.81	0.44, 1.50	0.502
BMI (kg/m^2)	1.04	1.02, 1.06	<0.001
PA (MET hours/week)			
Moderate/vigorous (≥10 MET hours/week)	1.07	0.74, 1.54	0.712
Having Diabetes	1.52	1.10, 2.10	0.011
Using insulin	1.56	1.09, 2.25	0.016
Using diabetes medication other than insulin	1.02	0.73, 1.41	0.918
Using hypertension medication	1.08	0.75, 1.57	0.678

Note. PA= Physical activity, MET=metabolic equivalent, QR=Qatari Riyal

Values are prevalence ratios and 95% confidence intervals based on Poisson regression.

[a] Significance in Poisson regression

Dietary patterns and depression symptoms in Poisson regression.

A Poisson regression was used to assess the association between dietary patterns and moderate to severe depression symptoms. According to the univariate analysis (crude model), participants in T3 (highest intake) of the “unhealthy” pattern had a higher prevalence of moderate to severe depression symptoms (PR=2.62; 95% CI: 1.71, 4.02) than participants in T1 (lowest intake). However, we did not find a significant association between the “prudent” pattern and moderate to severe depression symptoms in the crude model (Table5). In Poisson regression models, a significant positive association between the “unhealthy” pattern and moderate to severe depression symptoms was identified (Table 5). After adjusting for sociodemographic, lifestyle, and chronic condition variables, individuals in T3 of the “unhealthy” pattern showed a substantially greater prevalence of moderate to severe depression symptoms (PR =2.00; 95%CI: 1.27, 3.15) compared to individuals in T1. On the other hand, no significant association between the “prudent” pattern and moderate to severe depression symptoms was observed in the final model (Table 5).

Table 5. Association between Dietary Patterns and Depression Symptoms among Adults in Qatar (n=1000) [a]

Moderate to severe depression symptoms	Unhealthy pattern						Prudent pattern					
	T1	T2		T3		P trend [b]	T1	T2		T3		P trend [b]
Crude	1.00	1.58	(0.99, 2.52)	2.62	(1.71, 4.02)	<0.001	1.00	0.45	(0.30, 0.69)	0.66	(0.46,0.94)	0.348
Model1‡	1.00	1.44	(0.90, 2.31)	2.10	(1.33, 3.31)	<0.001	1.00	0.49	(0.32, 0.74)	0.76	(0.52, 1.09)	0.779
Model2§	1.00	1.39	(0.87, 2.24)	2.05	(1.30, 3.24)	<0.001	1.00	0.49	(0.32, 0.74)	0.75	(0.52, 1.09)	0.793
Model3‖	1.00	1.37	(0.85, 2.20)	2.03	(1.28, 3.20)	<0.001	1.00	0.48	(0.32, 0.73)	0.74	(0.52, 1.07)	0.717
Model4¶	1.00	1.34	(0.84, 2.14)	2.00	(1.27, 3.15)	<0.001	1.00	0.48	(0.32, 0.73)	0.81	(0.57, 1.15)	0.838

Note. [a] Data from Qatar Biobank. Values are prevalence ratios and 95% confidence intervals. Two dietary patterns were derived from factor analysis based on Eigenvalue >1, and items with factor loading |≥ 0.30|, scree plot, and interpretability based on Qatar food culture.

[b] Significance in Poisson regression

‡ Model 1: adjusted for sex and age (continuous).

§ Model 2: additionally adjusted for smoking, education, physical activity, and on diet.

|| Model 3: additionally adjusted for diabetes.

¶ Model 4: additionally adjusted for BMI (continuous), Hypertension medication.

Sensitivity analysis

Table 6 shows that a significant higher score on the unhealthy dietary pattern were significantly associated with higher depressive symptom score. However, no association between prudent pattern and depressive symptom score was found.

Table 6. Association between Dietary Patterns and PHQ-9 score as a continuous variable among Adults in Qatar (n=1000) [a]

Depression symptoms	Unhealthy pattern						Prudent pattern					
	T1	T2		T3		P trend [b]	T1	T2		T3		P trend [b]
Unadjusted	1.00	0.05	(-0.01, 0.10)	0.13	(0.07, 0.18)	<0.001	1.00	-0.10	(-0.16, -0.05)	-0.07	(-0.12, -0.01)	0.245
Multivariable adjusted	1.00	0.41	(-0.25, 1.07)	1.27	(0.58, 1.97)	<0.001	1.00	-1.21	(-1.87, -0.54)	-0.55	(-1.23, 0.12)	0.529

Note. [a] Data from Qatar Biobank. Values are regression coefficients and 95% confidence intervals. Two dietary patterns were derived from factor analysis based on Eigenvalue >1, and items with factor loading |≥ 0.30|, scree plot, and interpretability based on Qatar food culture.

[b] Significance in linear regression

Multivariable model adjusted for sex and age (continuous), smoking, education, physical activity, on diet, diabetes BMI (continuous), Diabetes medication other than insulin, Insulin use, Hypertension medication.

Interaction analyses

In Table 7, the subgroup analyses were adjusted for sociodemographic, lifestyle factors, and chronic conditions (model4). There was a significant positive association between the "unhealthy" dietary pattern and moderate to severe depression symptoms in those with diabetes (PR= 1.41; 95 % CI 1.28, 1.56; p-value <0.001), but not in those without diabetes (PR= 1.13; 95 % CI 0.92, 1.39; p-value= 0.233). However, the interaction was not statistically significant (p for interaction = 0.101). For the "prudent" dietary pattern, we did not observe an interaction between the pattern and diabetes.

There was a joint effect of unhealthy dietary pattern and diabetes on depression symptoms (fig.2A). Compared with those with a low intake of unhealthy dietary pattern and without diabetes, those with diabetes and had a high intake of unhealthy dietary pattern had the highest prevalence of moderate to severe depression symptoms (PR = 2.33; 95%CI 1.29, 4.22).

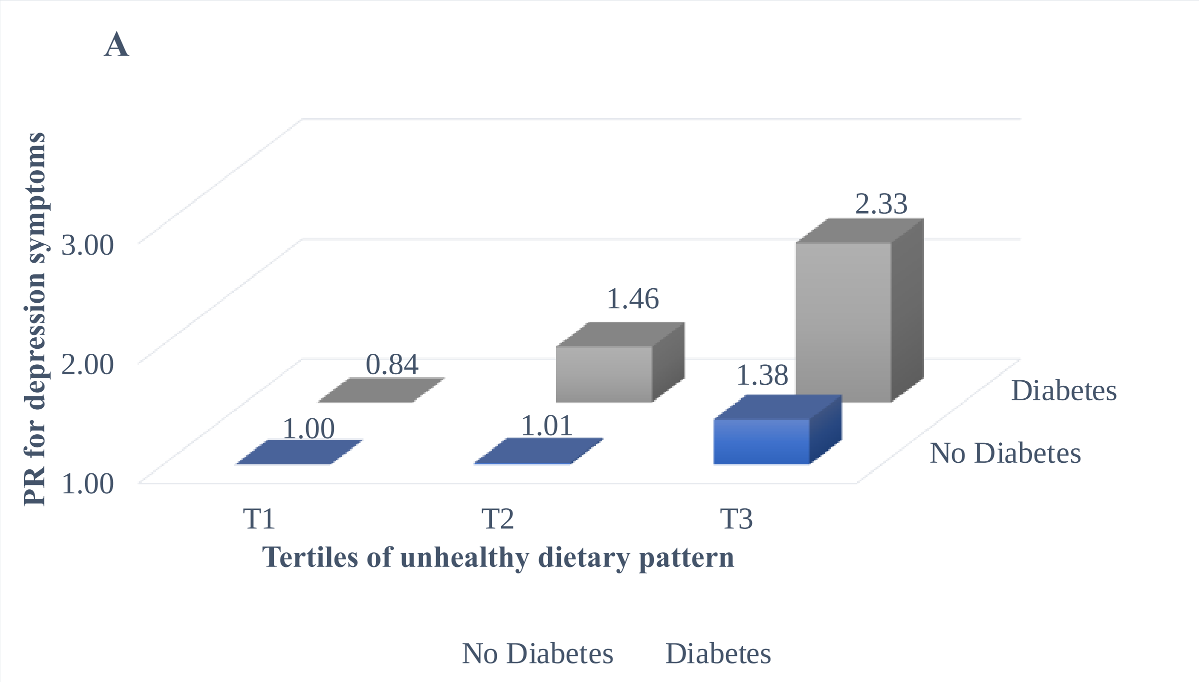
Table 7. Subgroup Analysis of the Association of “Unhealthy” and “Prudent” Dietary Patterns Scores with Depression Symptoms

Subgroup	Unhealthy pattern				Prudent pattern			
	N	PR	95% CI	P interaction [a]	N	PR	95% CI	P interaction [a]
Diabetes				0.101				0.094
No	488	1.13	0.92, 1.39		488	0.80	0.57, 1.11	
yes	511	**1.41**	**1.28, 1.56**		511	1.10	0.92, 1.32	

Note. Values are prevalence ratios (PR) and 95% confidence intervals based on Poisson regression. PR, adjusted for sex, age (continuous), smoking, education, physical activity, on diet, BMI (continuous), and Hypertension medication.

[a] Significance in Poisson regression

Bold= P-value significant.



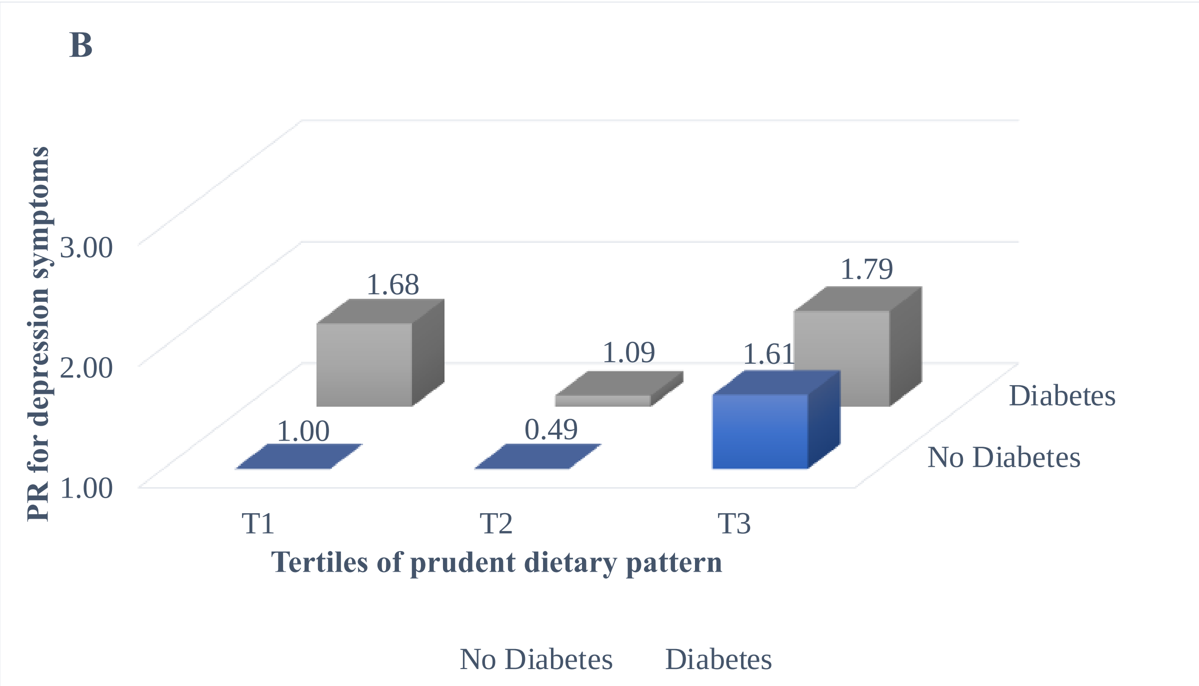


Figure 2. Joint effect of moderate to severe and (A) "unhealthy" dietary pattern and (B) "prudent" dietary pattern on diabetes.

Note. Prevalence ratio adjusted for sex, age (continuous), smoking, education, physical activity, on diet, diabetes, BMI (continuous), and Hypertension medication.

Chapter 5: Discussion

In this cross-sectional study of 1000 adults with and without diabetes in Qatar, we identified two major dietary patterns by factor analysis: “unhealthy” and “prudent” dietary patterns. The “unhealthy” pattern was characterized by a high consumption of fast food, Biryani, mixed dish (meat/chicken/fish), croissant, soft drinks, lasagna, and white bread. While the “prudent” pattern was characterized by a high consumption of fresh fruits, salads/raw vegetables, canned/dried fruit, and dates, fresh fruit juice, salads and cooked vegetables, brown bread, and soups/starters. The prevalence of moderate to severe depression symptoms was high in the sample, especially among those with diabetes. A high intake of “unhealthy” pattern among individuals with diabetes was associated with an increased prevalence of moderate to severe depression symptoms.

Prevalence of depression symptoms

The high burden and associated factors of diabetes observed in the current study were supported by other studies. Moderate to severe depression symptoms were seen in 13.5 % of participants overall (16.2% of participants with diabetes and 10.7% of participants without diabetes). Additionally, 12.1% of people with diabetes reported having moderate depression symptoms, while 4.1% reported having moderately severe to severe depression symptoms. However, among those without diabetes, 7.8% reported having moderate depression symptoms and 2.9 % reported having moderately severe to severe depression symptoms. Moreover, in the univariate analysis, we found that having diabetes was significantly associated with moderate to severe depression symptoms. This is consistent with the literature, which shows that depression has been associated with a number of chronic illnesses, including diabetes.(111) Indeed, previous studies have revealed that people with diabetes have a 2–4 times higher risk of depression than people without diabetes.(112) Males and those over the age of 50 had a lower prevalence of moderate to severe depression symptoms in this study, which is similar with findings from a German study.(113) On the other hand, those who had diabetes, were on insulin, or had a higher BMI had a higher prevalence of moderate to severe depression symptoms, which is also consistent with the literature.[114, 115]

Dietary patterns and depressive symptoms

In this study, the two identified dietary patterns were comparable to previously identified patterns in Qatar and the Middle East region. [18, 116-118] A previous study in Qatar also corroborated the relationship between age and dietary patterns. For instance, younger participants were more likely to follow the "unhealthy" dietary pattern, but those following the "prudent" pattern were more likely to be older participants.[18] Numerous studies have demonstrated that individuals with depression consume more unhealthy meals and fewer fruits and vegetables.[119] However, there is a lack of studies on dietary patterns in Qatar. Furthermore, the identification of dietary patterns is sample-dependent as it is a data-driven approach. However, the clustering of food items consumed is in line with other studies in the region.[18]

The findings of the current study are consistent with earlier studies, which have found a positive association between western/unhealthy diet and the risk of developing depression.[16, 61, 79, 86] A meta-analysis study published in 2017 included 21 studies from 10 countries including 117,229 people. Based on the study, the Western/unhealthy eating pattern, which is defined by a high consumption of processed and/or red meat, high-fat dairy products, refined cereals, and, sweets was associated with an increased risk of developing depression (OR=1.18; 95% CI: 1.05, 1.34; P=0.006).[16] Moreover, a meta-analysis published in 2014 found a trend toward a positive association between increased intake of the "Western" dietary pattern and the incidence of depression, though this association was not statistically significant (OR= 1.17; 95% CI: 0.97, 1.41; p-value= 0.094).[60]

We did not find an overall association between the "prudent" pattern and moderate to severe depression symptoms, which is not consistent with most of what was found in the literature. In the meta-analysis mentioned above, there was clear evidence that people in the highest category of healthy eating pattern had a lower incidence of depression than those in the lowest category (OR=0.64; 95% CI: 0.57, 0.72; p-value < 0.00001).[16] Furthermore, Rahe et al. found that a healthy diet consisting of a high consumption of fruits and vegetables, whole grains, and seafood was associated with a lower incidence of depression.[120]

Due to the fact that dietary pattern analysis evaluates the overall diet rather than individual components or foods, this strategy considers actual food and nutrient intake. However, because there are various possible nutrient content overlaps across dietary patterns, this strategy cannot determine the exact nutrients that are causing observed variations in disease risk. As a result, the ability of dietary pattern analysis to provide information on the biological associations between diet components and illnesses may be limited.[82] However, the findings of this study are consistent with earlier epidemiologic studies that found links between particular nutrient and dietary intakes and depression. In particular, higher consumption of fast food, refined grains (e.g., croissants, white rice, and white bread), and soft drinks has been associated with depression.[80, 121, 122]

A variety of factors could explain the disparities in the study's findings. Among these factors are the study designs, which varied in terms of depression assessment tools (i.e., self-reported scale vs. clinical diagnosis) and diet assessment tools (i.e., FFQ, diet history questionnaires, or 24-hour dietary recalls). In addition, the participants' inclusion and exclusion criteria, as well as the covariates used in the statistical models.

Potential mechanism of the association between dietary patterns and depression.

Diet and depression risk may be linked due to multidimensional biological effects. A less healthy diet (similar to our unhealthy diet) is typically high in calories, saturated/trans-unsaturated fatty acids, and sugar. These components are associated with depression, and this association can be explained by many factors, including inflammation, oxidative stress, gut microbiota, “hypothalamic–pituitary–adrenal” (HPA) axis, adult hippocampal neurogenesis and “brain-derived neurotrophic factor” (BDNF), tryptophan, and obesity.

Inflammation

Around 25% of people with neuropsychiatric illnesses, such as depression and schizophrenia, have elevated inflammation levels.[123, 124] Healthy eating patterns have been shown to reduce inflammation, which may be related to mental health issues. Clinical trials and longitudinal studies show that eating healthy, like the Mediterranean diet, reduces systemic inflammation.[125-127] Numerous nutritional components of a healthy dietary pattern have been shown to reduce the level of inflammation. For example, polyphenols, which are found in cocoa, curcumin, and blueberries, have potent anti-inflammatory properties that may help with a variety of neuropsychiatric disorders.[128] Omega-3 and polyunsaturated fatty acids, which are abundant in seafood like salmon, have anti-inflammatory effects that may delay the onset of depression.[129]

On the other hand, consumption of high-calorie, high-saturated fat foods appears to activate the immune system [130, 131]. Indeed, the inflammatory consequences of a high-calorie, saturated-fat diet have been postulated as one way in which the Western diet may harm brain health, including cognitive decline, hippocampal dysfunction, and blood-brain barrier damage[131]. Given that increased inflammation has been related to a variety of mental health problems, including mood disorders[132], this process also provides a method through which a poor diet may raise the risk of depression. This theory is backed by observational studies, which indicate that people with depression are more likely to consume foods associated with inflammation, such as trans fatty acids and refined carbohydrates. While they consume less nutritious foods with anti-inflammatory characteristics (e.g., omega-3 fats).[133, 134] Thus, changing the proinflammatory diets commonly linked with mental diseases to healthier diets could provide a unique approach to treating the inflammatory state associated with the emergence and severity of psychological disorders.

Oxidative stress

Oxidative stress, a situation in which oxidative and antioxidant processes are out of balance, can cause damage to a cell's DNA, lipids, and proteins. Persistent oxidative stress has been shown to play a role in depression or other mental disorders.[78] By decreasing or increasing dietary antioxidants, the diet can either exacerbate or alleviate oxidative stress. According to animal studies, Western diets appear to increase signs of oxidative stress in the brain.[135, 136] Because of the increased oxidative stress load found in people suffering from mental disorders[78], enhancing food quality may be a useful intervention for restoring antioxidants that have been depleted. The high antioxidant content of fruits and vegetables (e.g., vitamin C, vitamin E, and other carotenoids) may provide helpful protection against depression. Since it is well known that oxidative stress damages neurons, particularly in the hippocampus, which has been linked to depression, studies have found that increasing antioxidant levels helps reduce oxidative stress.[61, 137]

The gut microbiota

The microbiota–gut–brain axis has been implicated in the regulation of physiological processes such as cognitive function, neuropsychiatric diseases, and behavior, according to a rapidly developing body of literature.[138] Numerous mechanisms involved in depression pathophysiology (for example, inflammation[139], tryptophan metabolism[140], and neurogenesis[141]) may be influenced by the gut microbiome, given that it is one of the first body systems to interact with ingested food. Short-term food intake as well as long-term dietary habits are known as significant variables that affect gut microbiota composition, and diversity.[142, 143] Few human data exist to date, with just one uncontrolled dietary intervention showing that a diet rich in inulin-containing vegetables raised Bifidobacterium and improved satiety and intrapersonal competence levels, but had no effect on perceived stress or mood.[144] Recently, a study found that bacterial taxa enhanced by a one-year Mediterranean diet intervention were related to lower levels of inflammatory markers (Interleukin-17 and CRP) and better cognitive function in elderly adults.[145]Individual nutrients' impacts on brain health (e.g., fiber, polyphenols, and polyunsaturated fatty acids) may also be mediated directly through their effects on the gut microbiota.[146, 147]

The "hypothalamic–pituitary–adrenal" (HPA) axis

The HPA axis regulates glucocorticoid production and has been linked to the pathophysiology of neuropsychiatric disorders. It is made up of the brain (hypothalamus), adrenal glands, and pituitary. There are abnormalities in the HPA system or excessive cortisol production in over 60% of people with depression.[148] In healthy individuals, the cortisol response to acute physiological stress was shown to be reduced in clinical intervention studies using nutrients like vitamin C.[149] Studies on the effects of omega-3 fatty acids on cortisol levels in healthy and people suffering from depression have shown improvements in both populations.[150, 151] Furthermore, polyphenol-rich foods like dark chocolate and pomegranate juice have been shown in intervention studies to lower cortisol levels in healthy people.[152, 153] On the other hand, according to a meta-analysis, sugar-sweetened beverages with a high added sugar content, particularly fructose, were associated with an increased risk of depression.[122] This was supported by an animal experiment, which revealed that rats fed a high-fructose diet during preadolescence displayed greater anxiety and depressive-like behavior in adulthood, as well as enhanced HPA axis reactivity, resulting in glucocorticoid increases. Moreover, sugar-sweetened beverages contribute to obesity, and obesity may contribute to the development of depression by activation of the HPA axis.[154] It remains unclear how diet affects cortisol and other HPA-axis related measurements, but it is possible that dietary changes modulate the proinflammatory response to hypothalamic activation after psychological stressors.[155]

Adult hippocampal neurogenesis and "brain-derived neurotrophic factor" (BDNF)

Memory, learning, and mood regulation are all handled by the hippocampus, which is a crucial part of the limbic system.[156] BDNF is a neurotrophin that is abundantly expressed in the hippocampus and plays an important role in cellular activities like cell metabolism and synaptic plasticity that underpin both normal behavior and neuropsychiatric disorders. Furthermore, BDNF is the prototypical molecule that exemplifies the influence of food, antidepressant therapies, and exercise on depressive- and anxiety-like behaviors.(157) Serum BDNF levels have been found to be lower in people with major depression, and some experimental evidence supports BDNF's protective role against the development of depressive disorders.(158-160) There is substantial evidence that diet affects BDNF and the regulation of adult hippocampus neurogenesis.(161) Western-style meals heavy in fat and sucrose have been shown in animal models to impede neurogenesis, reduce BDNF levels in the hippocampus, and negatively affect cognitive performance.(162) On the other hand, substantial evidence from animal studies shows that dietary components like probiotics, vitamins, and omega-3 fatty acids have a positive effect.(163, 164) Certain polyphenol compounds, like cacao, blueberries, green tea, and curcumin, have also been demonstrated to counteract negative alterations and protect the integrity of adult hippocampus neurogenesis during situations of psychopathology, disease, and aging.(165) Observational studies give additional support, including documented direct correlations between healthy diets and greater hippocampus volume.(166-168) In a subgroup study of participants with depression at baseline, those who were randomly assigned to a Mediterranean dietary pattern supplemented with nuts had greater levels of plasma BDNF at the three-year time period than those who received the control intervention.(169) In comparison, a recent human intervention study showed that the Western diet can adversely impact hippocampal-dependent learning and memory.(170) Lastly, other pathways such as inflammatory pathways and the gut microbiota can influence neurogenesis, implying that additional dietary factors may affect neurogenesis indirectly through modulation of these secondary pathways, as previously mentioned.

Tryptophan

Tryptophan is a critical building component for a variety of crucial neuroactive molecules, which is an essential amino acid that must be obtained from food.[171] Tuna, peanuts, bananas, milk, chocolate, and chicken are all high in tryptophan.[172] Understanding the availability and metabolism of tryptophan may be important when using dietary interventions to treat or prevent mental disorders. For instance, increasing protein consumption can result in an increase in tryptophan availability, whereas carbohydrate intake might have an effect on free tryptophan levels.[173, 174]Where it was determined that meals containing carbohydrates are associated with higher secretion of insulin, which facilitates the transport of tryptophan, the building block of serotonin, in the brain and leads to a higher synthesis of serotonin, a hormone responsible for both increased mood and suppressed appetite.[175] Consequently, some authors believe that carbohydrate intake can boost moods or even alleviate depression.[176] This is contrary to longitudinal research, where it was found that dietary habits with a high glycemic index and load (e.g., meals high in refined carbs and sweets) may have a negative impact on psychological well-being and increase the risk of depressive symptoms.[121] Furthermore, observational research has identified a link between recurring hypoglycemia (low blood sugar) and mood disorders.[177] However, such benefits appear to be mediated by psychological mechanisms rather than by carbohydrates' nutritional characteristics. Consumption of a high carbohydrate diet or a diet with a high glycemic index has been linked in the short term to quick and immediate alterations in serotonin levels and, as a result, alleviation of some psychiatric symptoms (e.g., in premenstrual syndrome).[178] However, these findings cannot be immediately generalized to a condition with a longer duration and a longer induction period, such as major depression. Indeed, diets with a low glycemic index and/or glycemic load have been associated with a decreased risk of heart disease[179], conditions with a similar course, and most likely a comparable onset period to depression. Because refined carbohydrates are extensively processed, they are depleted of fiber, vitamins, minerals, phytonutrients, and essential fatty acids, causing rapid fluctuations in blood glucose and insulin levels.[180]

Obesity and its role in depression symptoms

The bidirectional and complex relationship between diet, mood disorders, and obesity is a result of a number of different factors.[181] In our study, we noticed that depression symptoms positively and significantly increased with an increase in BMI. According to a meta-analysis, men and women with obesity have a 55% higher risk of experiencing depression, whereas those suffering from depression have a 58% higher risk of developing obesity.[182] According to recent research, the interaction between nutrition, mental disorders, and obesity may be mediated by a number of interrelated mechanisms.[183] One mechanism is the HPA axis, which has been linked to both mood disorders and obesity due to its dysregulation, hyperactivity, and excessive glucocorticoid production and secretion. [183] Additionally, after exposure to a diet high in fat, decreased levels of several neurotransmitters (including serotonin) that are important in regulating neurological reward circuitry, mood, and dietary intake have been found.[183] Chronic stress and hyperactivation of the HPA axis may result in the excessive intake of Western diets and subsequent obesity in an attempt to alleviate stress-related anxiety.[184] This is similar to what we discussed previously, where sugar-sweetened beverages contribute to obesity, which in turn may contribute to the development of depression via activation of the HPA axis.[154] It was found in a cross-sectional study that obesity mediates the link between depression symptoms and inflammatory markers (such as CRP and IL-6), given the presumed causality of links connecting depression to increased adiposity and heightened inflammation levels.[185] As it was found that weight gain has been linked to increased rates of relapse and delay recovery in people receiving treatment for mental disorders, which may be due to obesity's inflammatory effects.[186, 187] Weight loss and Caloric restriction diets have shown promise in reducing inflammatory state and depression symptoms in overweight people.[188-190]

Depressive symptoms and diabetes

Numerous lines of evidence indicate that diabetes and depression have a bidirectional link. Indeed, a diabetes diagnosis raises the likelihood of developing depression. In comparison, depression is a well-known risk factor for diabetes in people without diabetes, and it leads to poor glycemic control and hastens the onset of complications in people with diabetes.[21, 22] According to our findings, the prevalence of moderate to severe depression symptoms among those with and without diabetes was 16.2 % and 10.7 %, respectively, based on the PHQ-9. According to the findings, among individuals with diabetes, there were 5.5% excess cases of having moderate to severe depression symptoms compared to those not having diabetes. Bawadi et al. found that the prevalence of depressive symptoms (PHQ-9≥10) among T2DM participants in Qatar was 15.4 %[11], which is roughly similar to what we observed. Additionally, a meta-analysis of 24 studies found that diabetes was associated with a 28% increased risk of depression.[22] However, in this the study, we found a much higher prevalence of having depression symptoms among individuals with diabetes, who had a 52% increased prevalence of suffering from moderate to severe depression symptoms compared to individuals without diabetes. Based on the literature, the bidirectional relationship between depression and diabetes is defined by a variety of characteristics, one of which is inflammatory biomarkers. In a cross-sectional study, CRP and the ratio of HMW/total adiponectin in T2DM patients, as well as sICAM-1 in type 1 diabetes patients, were found to be positively associated with depressive symptoms.[26] However, after multiple adjustments, only the association between HMW/total adiponectin and depressive symptoms persisted significantly among T2DM participants. We were unable to study the association between CRP and depression symptoms in this study because we only had CRP data for 104 people.

In the current study, we discovered that the use of insulin among people with diabetes was considerably high (i.e.,31.3 %) (data not shown). We noticed that insulin use was significantly associated with an increased risk of moderate to severe depression symptoms in the univariate analysis. This is consistent with the literature; in a meta-analysis study, insulin therapy was associated with an increased risk of depression incidence in both crude (OR=1.59, 95% CI: 1.41-1.80, p-value <0.001) and adjusted data (OR=1.41, 95% CI: 1.13-1.76, p-value=0.003).[114]

The role of diabetes on the association between dietary patterns and depressive symptoms

In this study, we hypothesized that there is an association between "unhealthy" dietary pattern and depressive symptoms severity, which is stronger among those with diabetes than those without diabetes. Results from data analysis support our hypothesis. We observed that people with diabetes and had the highest intake of "unhealthy" dietary pattern had the highest prevalence of moderate to severe depression symptoms than people without diabetes who consumed the lowest intake of "unhealthy" dietary pattern (PR = 2.33; 95%CI 1.29, 4.22). However, there was no significant association between the "prudent" pattern and moderate to severe depression symptoms stratified by diabetes status. Akbaraly et al.[61], showed that a high intake of fried food, processed meat, sweetened desserts, high-fat dairy products, and refined grains is associated with depressive symptoms. In that study, the prevalence of diabetes was significantly higher among participants with depressive symptoms compared to those without.[61] This is consistent with what we found. T2DM is commonly associated with an unhealthy lifestyle that includes inactivity, unhealthy diet, and being overweight.[191] In a large cross-sectional study of the Norwegian population, individuals with type 1 and type 2 diabetes reported lower levels of exercise and a higher BMI than those without diabetes.[192] It is comparable to what we found in the current study in terms of BMI, but there were no differences in exercise levels between the two groups (data not shown). These lifestyle factors can be considered as an unspecific source of stress that disrupts the body's homeostasis and thus increases the risk of depression.

Diet modification is a cornerstone of diabetes and depression management. Ajala et al.[193] performed a meta-analysis to determine the effect of various diets on glycemic control, lipids, and loss of weight in patients with T2DM. The study analyzed 20 randomized controlled studies that lasted at least six months and involved 3,073 participants. High-protein, Low-carbohydrate, high-fiber, vegetarian, vegan, low-glycemic, and Mediterranean diets were compared against low-protein, "American Diabetes Association" (ADA), "European Association for the Study of Diabetes" (EASD), low-fat, and high-glycemic diets as controls. A greater loss of weight was observed on the Mediterranean (−1.84 kg, $P < .001$) and low-carbohydrate diets (−0.69 kg, $P = .21$). [193] In comparison to the control diets, the greatest reductions in HbA1c level were found in the Mediterranean (−0.47%, $P < .001$), high-protein (−0.28%, $P < .001$), low-glycemic (−0.14%, $P= .008$), and low-carbohydrate diets (−0.12%, $P = .04$). All diets, with the exception of the high-protein diet, raised HDL-C levels. [193] Moreover, in an RCT with 115 adults with T2DM and obesity, the effect of a low-carbohydrate diet [14% of energy as carbohydrate] was compared with a high-carbohydrate diet [53% of energy as carbohydrate] (low-glycemic foods), combined with physical activity.[194] After a year of follow-up, it was found that the low-carbohydrate diet resulted in lower diabetes medication requirements, greater improvements in the lipid profile, and blood glucose stability, implying an effective strategy for optimizing T2DM management. However, both groups experienced comparable mean weight loss [low-carbohydrate diet: −9.8 kg and high-carbohydrate diet: −10.1 kg]. [194] The same sample was studied in another study for 2 years to examine the long-term effects of low and high carbohydrate diets on psychological health.[195] There were no differences between the groups for the changes in any psychological health outcome. Over time, improvements in "Beck Depression Inventory" (BDI), "Profile of Mood States" (POMS), ["Total Mood Disturbance" (TMD); four subscales], "Problem Areas in Diabetes" (PAID), and "Diabetes-39" (D-39) scores occurred (p-value ≤ 0.05). Moreover, significant improvements in BDI, POMS (TMD; two subscales), D-39, SAI, and PAID scores were associated with weight loss and lower HbA1c levels (p-value <0.05). Weight loss appears to be the main driver of these changes, and these findings imply that various healthy dietary patterns can be used as long-term dietary management methods for obesity and T2DM, thereby improving diabetes patients' mental health.[195]

Because the data in this study is cross-sectional in nature, it is impossible to determine the temporal nature of the correlations between these three variables. Diabetes may mediate the link between a high-sugar diet and depression. Specifically, a high intake of sugar increases the risk of developing diabetes, which increases the risk of developing depression.[121] In spite of that, there is a theory that holds that individuals suffering from atypical depression have an increased appetite, particularly for high-fat, high-sugar meals and less nutritionally balanced diets, which leads to an increase in glucose production over time.[196] There is evidence that unhealthy "western" diets are linked to an increased risk of depression[61, 79, 197], and the detrimental effect of western diets (high in saturated fat and refined carbs) on the brain, as well as obesity, is well documented.[162] As a result, unhealthy diets may be a significant risk factor for diabetes as well as depression.

Strength and limitations

The main limitation is the cross-sectional study design. Although we cannot claim causation, the findings are in line with the current knowledge and suggest the importance of diet in the prevention/management of both diabetes and depression. It provides direction of future research. Compared with medical intervention, lifestyle intervention including dietary modification is cost effective and has long term benefit. The second limitation is that we could not adjust for energy intake in the analyses due to the use of FFQ, since amounts of foods consumed could not be obtained. Nevertheless, the FFQ can be used to classify people in large-scale epidemiological studies in order to reflect their typical long-term intake. The relative validity of the FFQ employed in the EPIC study has been demonstrated.[198]The third limitation is that the two patterns explained only 26.2% of the variance. However, in population-based studies, it is common that dietary patterns using factor analysis explain only a small proportion of the variation of the entire diet. The amount of variance that is explained by dietary patterns varies according to the number of food groups used in their construction. As the number of food groups increases, the variance explained by dietary patterns decreases. In our study, we used 38 food groups in our analysis, which is similar to the study done before in Qatar.[18] These 38 food groups best represent the foods consumed most frequently in Qatar. The fourth limitation is that depressive symptoms were self-reported using the PHQ-9, which is a screening tool, not a diagnostic tool for depression.

On the other hand, this study's main strength is that we used a comprehensive food consumption list of 102 food items, which captures the whole range of food consumption. Furthermore, we used detailed data about sociodemographic factors, lifestyle factors, and medications used, which enabled us to measure confounder factors.

Future directions

The factor analysis methodology used in this study should be replicated with a larger national sample. Using a larger sample size would allow us to conduct subgroup analyses on the association between individual food intake and depression. Moreover, a national sample would enable us to see if the results could differ based on diabetes control or diabetes duration. We would be able to include those under the age of 18 in this nationwide sample. Furthermore, additional research using longitudinal data is needed to better understand the bidirectional connections between depression symptoms and diets. We propose to use qualitative research to provide detailed information that will assist us in comprehending our quantitative results and may shed light on new areas of concern that require further investigation. Longitudinal studies with an adequate sample size are needed to investigate the mechanisms of how dietary patterns affect depressive symptoms and diabetes risk. Based on QBB study, future studies could use data linkage (through the primary health care system) and examine the association between dietary patterns and depression medication use.

Conclusion

In summary, we found that dietary patterns were associated with depression symptoms among adults in Qatar. However, these associations depend on health conditions. Among those with diabetes, the “unhealthy” dietary pattern was positively associated with depression. Promoting healthy dietary intake should be encouraged in the prevention of depression and the related health burdens.

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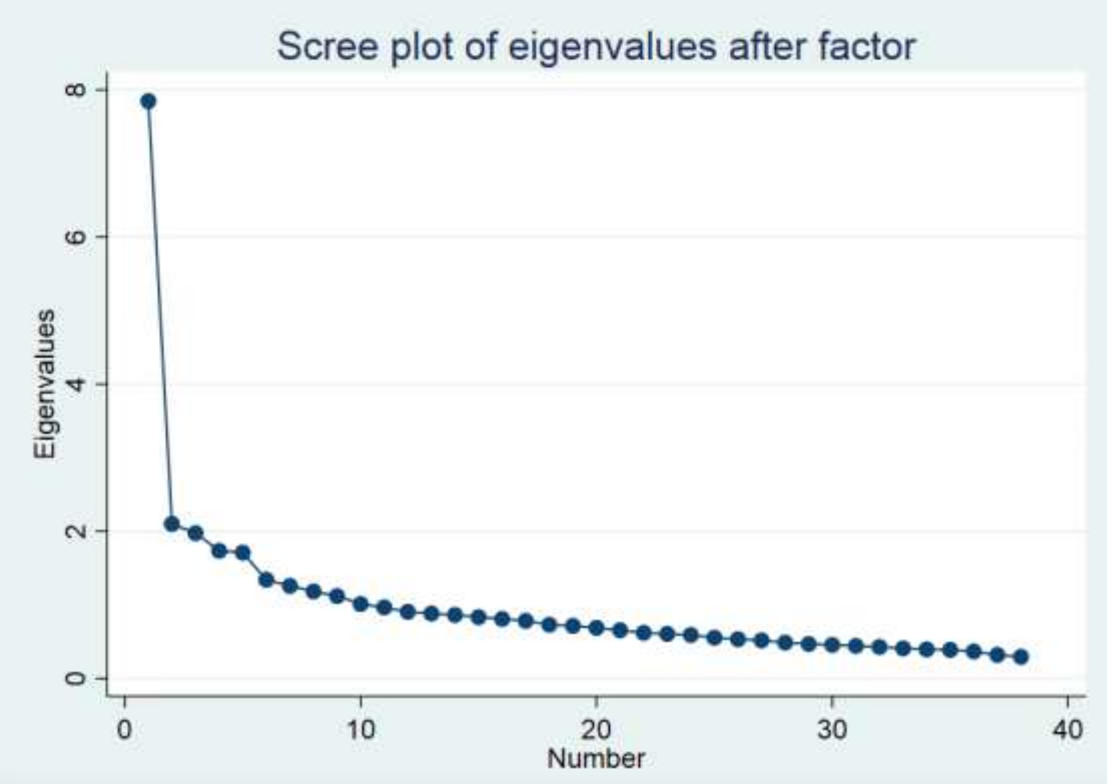
Appendices

Appendix A: Scree plot



Appendix B: QBB Approval Letter

qatarbiobank

Member of Qatar Foundation

QATAR BIOBANK INSTITUTIONAL REVIEW BOARD

Email: qbbresearch@qf.org.qa

QBB IRB MOPH Registration: IRB-QBB-2019-001
QBB IRB MOPH Assurance: IRB-A-QBB-2019-0017

Date	10/01/2021
Lead Principal Investigator	Ms. Noor Hamad- QU
Committee Action	Exempted approval
Approval Date:	10/01/2021
IRB Protocol #:	Ex -2021-QF-QBB-RES-ACC-00005-0149
Study Title	Effect modification of the association between dietary patterns and depression by diabetes among adults in Qatar: a population-based study
Expiration Date	10/01/2021 - 09/01/2022

Dear PI,

The above-referenced protocol has been granted exemption review as the Principal Investigator, Ms. Noor Hamad will only be reviewing de-identified, anonymous samples or data for the above-mentioned study title.

Exemption Category 3: Research involving the collection or study of existing data, documents, records, pathological specimens or diagnostic specimens, if these sources are publicly available, or if the information is recorded by the investigator in such a manner that subjects cannot be identified directly or through identifiers linked to the subjects.

Amendments: If you wish to change any aspect of this study, such as the procedures, the consent forms, or the investigators, please communicate your requested changes to the IRB. Any new procedure is not to be initiated until the IRB approval has been given.

It is the Principal Investigator's responsibility to obtain IRB review and continued approval before one month from the expiration date. You may not continue any research activity beyond the expiration date without approval by the Institutional Review Board.

Please retain a copy of this letter with your IRB approved protocol.

Sincerely yours,

Dr. Khalid Al- Ali
Vice Chairman, Institutional Review Board QBB

QBB- IRB, QF-QBB-RES-ACC-00005-0149, 10 Jan 2021 – 9 Jan 2022

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Appendix C: Food groups used in factor analysis

Food group	Food items included
Coffee	Arabic coffee, instant coffee, other coffee (e.g,. filter coffee, cappuccino)
Tea	Tea, herbal tea, Karak
Milk	Milk as a beverage (cold milk, cappuccino)
Milk added to cereal	Milk added to cereal
Milk shakes	Milk shakes or floured milk
Yoghurt	Laban, yoghurt, labneh
Cheese	Other white cheese (halloumi, cream cheese), processed cheese, hard cheese (such as gouda, cheddar)
Butter	Butter
Breakfast Cereal	Balaleet, cornflakes and other cold cereals, museli, porridge, other brand cereals
Arabic/Iranian bread	Arabic bread (lavash), Iranian bread
White bread	Toast (sliced bread, white)
Brown bread	Toast (sliced bread, brown)
Other bread	Other breads
Croissant	Croissant
Zaatar fatayer	Zaatar fatayer
Soups/starters	Ready-made soup from powder; other soups; hummus, mutabal, baba ghanush; other dips; tabbouleh; koussa mahshi (stuffed courgettes); eggplants fried or baked, moussaka; other vegetable starters; fish and seafoods starters; chicken, meat, or sausage starters
Salads and raw vegetables	Raw vegetables; Green leafy salad (e.g., lettuce); Mixed salad (for example with tomato, onion, cucumber, other vegetables); Fattoush; Beans salads (chickpeas, lentils); Bulghur salad
Salads and cooked vegetables	Vegetable stews; Vegetable curries; Other cooked vegetables; corn

Food group	Food items included
Potato	Potato
White rice	White rice
Biryani	Biryani
Asian noodle	Asian noodle
Lasagna	Lasagna
Red meat	Red meat
Chicken	Chicken
Fish	Fish
Chicken/meat fish mixed dish	Meat served with rice (Mashboos); Chicken with rice; Harees; Meat cooked with vegetables (Margooga, Saloona); Chicken cooked with vegetables (Margooga, Saloona); Meat curry; Chicken curry; Kofta; Meat kebab; Chicken kebab; Lamb chops, escalope; Grilled chicken
Grilled/fried/baked Fish	Grilled, fried or baked fish; Fish cooked with vegetables; Smoked fish;
Eggs	Eggs (boiled, fried, omelettes, scrambled)
Fast food	Meat shawarma, Chicken shawarma, Falafel wrap, Samosa, Other middle-eastern style fast foods, French fries, Potato chips, Burgers, hotdogs, Pizza, Fried chicken(e.g., wings, nuggets),
Fresh fruit	Fresh fruit, banana, watermelon
Canned/dried fruit and dates	Canned fruits, dry fruits, dates
Desserts	Traditional desserts (mahalabea, halwa, aquili, elgayemat, kammafaroursh); Other Middle Eastern or Lebanese desserts; Cookies, biscuits; Muffin, cake, doughnut
Chocolate	Chocolate
Ice cream	Ice cream
Nuts	Nuts
Fresh fruit juice	Fresh fruit juices; Smoothies
Soft drinks	Preserved fruit juice (canned/bottled); Soft drinks, sodas; Diet soft drinks, sodas; Energy drinks